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Nature of obesity : an etiological survey

Donald Ross

University of Nebraska Medical Center

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THE NATURE OF OBESITY
An Etiological Survey

Donald Ross
A.B. Grinnell College
1934

Announcement
Senior Thesis presented to the College
of Medicine, University of
Nebraska, Omaha
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INTRODUCTION

The purpose of this paper is to attempt an etiological survey of the subject of obesity with some attempt to correlate and classify this material. Most consideration will be given to the question of metabolism for obesity represents a disease, or more accurately, a disorder of metabolism. Metabolism is not accurately represented by the determination of the basal metabolic rate, the respiratory rate, the specific dynamic action and so forth because all these determinations depend on various calculations from respiratory gas exchange tests. These tests, though helpful, may be considered as no more and no less than an indication of metabolism. Metabolism is a much broader term. The definition of metabolism includes the sum total of all the building up (anabolic) and the tearing down (katabolic) processes occurring continually in our bodies.

Thus any consideration of metabolism must depend not only on basal metabolic rate determinations, but also include such factors as appetite, hereditary influences and the role played by endocrine balance. According to this concept it is obvious that obesity is a disease of metabolism, and it matters not whether that imbalance in metabolism is the result of perverted appetite or perverted

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endocrine balance. As DuBois (31) points out that obese persons are often lazy and strongly addicted to habits of overeating. Are not these very factors of laziness and self indulgence inborn tendencies dependent on heredity and emotional balance.

In this paper, also, the author will make some attempt to classify obesity. In most of the references, the questions of classification are carefully avoided. It seems to this author that classification is the most important part in the study of any disease. Even a temporary classification based on very incomplete knowledge is better than none at all. In this paper, then, as many as possible of the various methods of classification will be presented.

In outlining the scope of this work, it is the author's intention to include a short section on definition and standards, a short chapter on the chemistry of normal fat metabolism, before undertaking a discussion of the etiology and the metabolism of obesity. These last two sections are naturally very closely related. The author has had to arbitrarily say that this factor belongs under metabolism and that factor under etiology. Obviously a decreased metabolic rate could be considered as an etiological factor. As the writing

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progressed, the author found that it was impossible to establish a clear cut distinction between the two chapters. Consequently, the metabolic factors important in the etiology of obesity are listed briefly under the chapter on etiology and the experimental proof both pro and con are presented in the chapter on metabolism. The important question of treatment has been omitted entirely from this paper. It is hoped that this omission may not be construed to minimize its importance. A line must be drawn someplace according to the time available, and treatment was the most easy to eliminate because it is the least correlated with etiology and metabolism.

The present work represents a review of literary material only. Much of this was selected from the Quarterly Cumulative Index Medicus of the American Medical Association. To a lesser extent, material was obtained from other reference lists and bibliographies. Numerous books on the subject were also consulted in a further attempt to make as complete a survey as time would permit. The bibliography includes only such references as were available from the Library of the College of Medicine, University of Nebraska, Omaha. Much of the literature in foreign languages was necessarily excluded because of an inability to translate it, though

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wherever possible abstracts and translations were used. When translations were not available, foreign references of sufficient importance were included and due credit given in the bibliography to the source from which they were cited.

The author wishes to express his appreciation to the librarian and her staff for their kind assistance in finding many of the references, and to Dr. E. J. Kirk for his helpful advice and suggestions.

DEFINITION AND STANDARDS

Obesity comes from the English root obese which is derived from the Latin word "obesus" meaning to devour. Dorland (29) has defined it as "an excessive accumulation of fat in the body." He distinguishes between a hyperplasmic type, which consists of an increase in the body protoplasm only, and a hypoplastic type, which is characterized by a decrease in body protoplasm in addition to an increase in fat. This seems to imply that obesity may be either protoplasmic or adipose in nature so as to include any condition of overweight, but that when fatty in nature is associated with hypoplasia of the body protoplasm. Dorland lists corpulence and fatness as synonymous with obesity. We shall include adiposity, stoutness, overweight, and overnutrition as synonyms.

The difficulty with this definition lies in the word "excessive." As Graefe (45) points out that obesity should not be confused with overweightness. Obesity is too often diagnosed as the result of a calculation of a weight that is in excess of normal standards. Obesity is a disease. It represents a functional disturbance characterized by superfluous fat deposits. It does not matter theoretically or practically whether

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the surplus weight is great or small. Lambie (65) also believes that the word excessive should be interpreted as a pathological entity which interferes with functional activity. He points out that too often physicians are tricked into accepting artificial criteria for obesity. These are determined by individual taste and the dictates of fashion. Obesity does not occur until fat deposition reaches a point where it interferes with functional activity. A person may be said to be too fat, if the adiposity results in distress or discomfort, impairs the sense of well being or diminishes the capacity to enjoy life. Ultimately, the obesity may embarrass the heart and respiration and diminish the patient's resistance to disease, and so be a menace to life. The normal weight standards depend too much on random statistics. The normal weight for any individual should depend on the type of physical make up to which the patient belongs.

McLester (79) has attempted to set up a normal minimum limit for the word excessive. He says that the exact point at which obesity begins is hard to define but as a general rule, it can be said that a figure which is from 10 to 15% above the fixed standard

Definition and Standards

can be regarded as normal, while one that is 25% or more above this standard represents obesity. There are between these two figures, however, grades of overweightness which under some circumstances can be regarded as normal, and under others as abnormal. For instance, in heart disease, nephritis, or gout, a body weight which exceeds the normal by as much as 10% is excessive and therefore constitutes obesity.

McLester (79) also believes that a slight increase in weight with age is physiological. At the age 35, a gain of ten pounds, and at age 50, a further gain of 10 to 20 pounds is to be expected because of its constant occurrence. He presents a formula which approximately expresses such a physiological gain.

$$\text{Normal weight (kg.)} = \text{Height (cm.)} - 100$$

Although weight gain in adults is assumed to be normal in standard tables based on insurance statistics, Lambie (65) does not believe these are proper criteria from which to judge normal weight. He suggests the following formula.

Males

$$\text{Normal weight (lbs.)} = \frac{110 \text{ lbs}}{5 \text{ ft.}} + \frac{5.5 \text{ lbs}}{\text{Additional inches of height}}$$

Definition and Standards

Females

$$\text{Normal Weight (lbs)} = \frac{110 \text{ lbs}}{5 \text{ ft}} + \frac{5.0 \text{ lbs}}{\text{Additional inches of height}}$$

Lambie believes that the results calculated from these formulae should be expressed as a ratio:

Actual Weight

Ideal Weight

The normal ratio lies between 1 and 1.1. Values between 1.1 and 1.25 represent slight obesity. 1.25 to 1.50 is moderate obesity. Over 1.50 represent marked obesity.

Poulton (92) cites the formula of M. Flack (Biometrika 14/316/1922) for both sexes.

$$\text{Normal Wt. (Kg.)} = 0.408 \times \text{Ht. (cm)} + 0.693 \\ \times \text{Stem length (cm)} + 70.213$$

Dreyer (30) has considered body build of adults up to 50 years of age without reference to age on the basis of four measurements; height, sitting or stem length, chest girth, and vital capacity; each expressed by formulae in terms of the other and tabulated in tables to eliminate calculation for the determination of normal weights of each sex. However, the 1925 report of the Committee on Dreyer Measurements in relation to Life Insurance Underwriting Practice for the Association of Life Insurance Medical Directors (102) revealed that the

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Dreyer standards were inaccurate. They reported them as unsafe criteria for judging overweight risks because many of Dreyer's normals were distinctly abnormal according to insurance standards.

Obesity may also be defined on a qualitative basis. Rony (95) believes that obesity may exist without overweight because of a restricted diet. He designates this as "masked" obesity, and he explains it as an inherent obese tendency, which will become manifest whenever dietary restrictions are removed. He also describes "pseudo" obesity due to overfeeding and limitation of exercise. These individuals become thin again as soon as the overfeeding is stopped. Kisch (61) also uses the term "pseudo" obesity. He says that some patients present the appearance of obesity with an enlarged abdomen. This is due to a sympathetictonic inhibition of the movements of the bowels.

From the above, it may be seen that obesity should be defined as an excess percentage of fat deposition in the body, but from a practical standpoint, the total body weight is the only clinical means of determining the prescence of obesity. Graefe (45) indicates that though obesity passes as a disease of metabolism, it should really be called a disease of overnutrition.

NORMAL FAT METABOLISM

To understand why one person is of normal weight, another fat and a third lean, we must be familiar with some of the more important chemical processes occurring during the metabolism of the body. Therefore, we must consider the metabolism of fat in the normal person.

Fat Distribution

In the healthy human being of normal weight, approximately one sixth of that weight is fat stored as reserve material for a supply of energy to be called upon in case of need. Barker (2) says that a normal man weighing 70 kilograms will contain 12 kilograms of fat. Of this 9 kilograms will be stored in certain reserve areas or depots, thus preserving a potential combustion value of 80,000 calories or enough to cover the total energy requirements of the body for about a month. The normal depots of fat storage lie in the connective tissues of the trunk and the extremities, especially in the subcutaneous tissues. The distribution of the stored fat varies somewhat with sex and individuals. In males, the fat tends to be deposited in the subcutaneous tissue of the neck and of the abdominal wall. In females, the breasts, abdomen, buttocks, and thighs are the sites of predilection for fat storage.

Normal Fat Metabolism

Posture, also, is important. Kerr (60) points out that round shouldered individuals tend to store fat on the abdominal wall; women wearing high heels tend to store fat on the buttocks. Fat is also deposited in small amounts in the heart, kidney, muscles and liver.

Ingestion and Storage

The sources of body fat are the fat ingested in the diet and the fat derived from the metabolism of excess carbohydrate and stored as fat. Of these, transformation of carbohydrate is the most important. Lambie (66) says two thirds of the food ingested is carbohydrate.

The fats ingested are broken down into fatty acids and glycerol by the ferment lipase. The most common fatty acids ingested into the body are the triglycerides of oleic, palmitic, and stearic acid. When united with glycerol, to form triglycerides, the fatty acids are called neutral fats. Bloor (12) says it seem probable that the fats ingested, on absorption by the intestinal epithelium, are split by lipase ferment from the pancreas and the intestinal wall into fatty acids and glycerol. While in the intestinal wall these substances are again resynthesized to form neutral fat. The mechanism of this action is unknown, but it seem likely that lipase has a reverse action in that it can either split up

Normal Fat Metabolism

or synthesize neutral fat. Once absorbed, this fat is absorbed by the lacteals and carried to the lymphatics of the intestine, then to the thoracic duct, and finally to the blood stream.

Following the ingestion of fat, there is a rise in the blood lipoid content. Rony and Levy (98) called this alimentary lipemia. These authors report that after the ingestion of one pint of 20% cream, the peak of the blood lipoid curve is reached in about 3-5 hours. Jöslin (57) reports that the lowest fasting level is 120 mg%, the highest normal value after fat ingestion is 230 mg%.

Bloor (12) believes, since the liver is the only organ loaded with fat during absorption of this food-stuff and since the fatty acids of this fat are found to be of the same degree of saturation as those of the blood fat, that this organ is the site of the desaturation of the neutral fat of the blood. Tissue fat analysis has shown that it possesses a higher degree of unsaturation than does depot fat. Tissue fat also has undergone phosphorization. Bloor (12) believes these processes occur almost wholly in the liver. This fat is then deposited as complex cellular lipoids in the active tissues of the body (Heart, liver, kidney, muscle).

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Most of this is stored as phospholipids, but also as cholesterol and others. Bloor (12) called this type of deposited fat "active tissue complex cellular lipid." Maximow (77) says that there is also a masked or bound fat which is part of living protoplasm. It cannot be demonstrated microscopically but may be extracted chemically.

Regarding the storage of fat in the depots, Bloor (12) says that the fat must be deposited in some relationship with lecithin and cholesterol. As evidence for this view, he points out that lipase, the only ferment capable of hydrolysing neutral fat of the higher series, is found only in the intestine and pancreas. Hence re-synthesized neutral fat in the blood stream cannot be hydrolyzed by the tissues without undergoing some change. He believes that because of the coincident rises of lecithin and cholesterol with fat in the blood after a meal these substances must therefore take part in the metabolism as fat. Probably most of this fat is transformed into lecithin esterases.

In addition to unsaturation and taking on of phosphorous, the fatty acids are said by Musser (83) to bear a similar correspondence to the selection of amino acids for body protein in the building of body fat. In

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In this connection, Bloor (12) states that with a choice of food, the organism builds a depot fat characteristic of its species, but on a diet of selected animal fat, the same is stored unchanged in the fat depots of the body. However in poisoning, a mobilization of the fat occurs to the liver, where the fat is then converted to the type characteristic of the species.

Lambie (66) says that when depot fat is mobilized, this fat is again broken down into fatty acids and glycerol which are then resynthesized into neutral fat in the blood stream. This is essentially what happens in the absorption of food fat from the intestine. Joslin (57), however, says that depot fat is transported to the liver by lecithin and cephalin in the form of fatty acids. There is is desaturated and thus prepared for use in the body.

Regarding the conversion of carbohydrate to depot fat, Lambie (66) says that the glucose is synthesized to fat by the condensation of three molecules of glucose to form fatty acid which unites with glycerol to form fat. Protein normally becomes fat only to a small extent from the intermediary protein metabolism of glutogenic amino acids which are changed to carbohydrate form of triose to form hexose . This is less readily

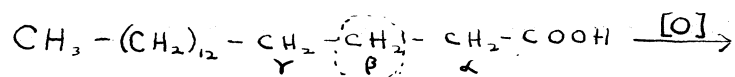
Normal Fat Metabolism

accomplished than its conversion into glycogen from which the glucose is then formed.

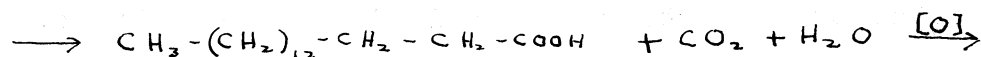
Utilization of Fat as Energy

Graefe (45) states that fat deposits serve three purposes; aid in heat regulation, anchor organs, and protect deep seated vital organs from mechanical injury. We might also add that fat serves as a source of nutritive material. DuBois (31) says depot fat represents the one perfect foodstuff for human consumption.

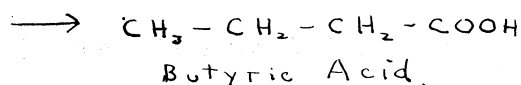
In spite of the rather uncertain mechanism of fat transportation and deposition in the body, the manner of actual oxidation of the fat to produce energy is better understood. Following are the formulae given by Dr. Morgulis in his lectures explaining the mechanism for the combustion of fat.



By Beta Oxidation to



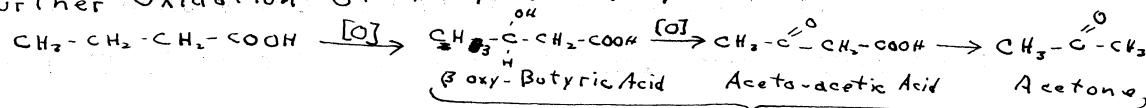
By repeated Beta Oxidation until we have



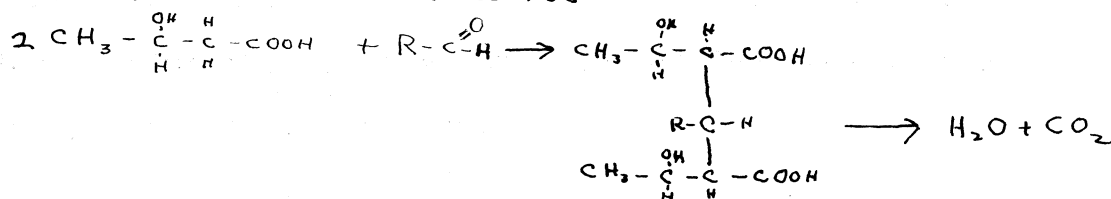
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Further Oxidation of Butyric Acid gives



However Butyric Acid reacts with a Carbohydrate molecule to form $\text{H}_2\text{O} + \text{CO}_2$ and prevents the formation of these Acid bodies



Bloor (12) states that the breaking down of fatty acids at the beta position involving two carbon atoms at a time is probable because most fat have been found to contain fatty acids with an even number of carbon atoms. He says the probability is even further increased because fats may be built up from carbohydrate through lactic acid, acetaldehyde, beta hydroxy butyric aldehyde, and finally, by simultaneous oxidation and reduction, to butyric acid. This process is repeated over and over until a long chain acid or fatty acid is built up. It is also well known that for the complete oxidation of fatty acids to carbon dioxide and water, the oxidation of carbohydrate is essential, so that actually as has been said, "Fats burn in the flame of carbohydrate."

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The heat value of one gram of fat, according to Rubner (100) is 9.3 calories. Rubner proved that food oxidized in the body gave off the same amount of heat per unit surface. Graefe (45) adds that all food stuffs are represented in nutrition in accordance with their caloric value whether they are derived from the diet or from substances of the body.

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Obesity may be said to always be due to overfeeding; in this connection overfeeding stands for an excess of nutritional calories above the amount actually required. It does not matter whether the requirement is normal, increased, or decreased. The body may be compared to an automatic furnace which burns up only the calories needed to supply the body with energy. The excess calories ingested are stored principally as fat.

The problem of the etiology of obesity, however, is not as simple as the above statement would indicate. Were it true, we might assume that all there is to the question of obesity is the determination of how much in excess the intake is over the outgo. The feature of modern civilization may be said to be excess nutrition. Food supplies have been steadily decreased by these same machines. Why then do we not all get fat? Only a small percentage of the population show any marked degree of obesity. Yet all of us consume in a single day nearly twice as much energy as food as we expend as work.

The problem of obesity then is the determination of what factors tend to allow the energy balance to become positive. In this section as well as in the following section on metabolism an attempt will be made to answer

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this question.

This section will include a discussion of the predisposing factors, a presentation of the question as to the exogenous or endogenous nature of obesity, and a detailed study of the factors contributing to development of both of these types of obesity.

Predisposing Factors

Age

There are times in the life of an individual when obesity is most likely to develop. Age is not the fundamental cause; endocrine activity, food intake in response to growth demands, variation in activity, mode of living, and many other conditions decide whether or not one is to be obese at a certain age.

Dunlop and Murray (34) in the report of 523 cases of obesity found that in females the onset of obesity was mostly between twenty to forty years (average thirty), and in males the onset was between forty and fifty years (average forty-two). Preble (93) gives the following table for the onset of obesity.

Age	0-10	11-20	21-30	31-40	41-50	51-60	61-70	71-	Total
Men	1	11	53	85	68	18	8		244
Women	7	65	178	238	196	62	10		756
Total	8	76	231	373	264	80	18		1000

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Christie (23) classifies obesity in respect to age. In infants the obesity seen is mostly of the exogenous nature. An excessive allowance of starch and sugar in certain proprietary foods results in some bottle-fed babies. Some mothers have milk that seems to be particularly rich, and their babies often become obese. Endogenous obesity due to a hypothyroid condition (cretinism) must always be ruled out. The growing child, like other growing young animals, is seldom fat. The child requires about 3,500 calories where the adult needs only 2,500 calories. The growing child also takes plenty of exercise. Nevertheless, obesity does sometimes occur and is most frequent around the time of puberty. Christie (23) says that roughly about three percent of the boys become stouter at this time and a slightly higher percentage of the girls. About fifty percent of these belong to the endogenous group and show signs of a pituitary or thyro-pituitary defect. The others are corpulent without altering their daily habits or without treatment.

There are two periods in a man's life when he tends to gain weight. Christie (23) states that men become fat when they give up athletic lives to enter business, perhaps to marry and start a home of their own; or when, after attaining worldly prosperity, they begin to "ease

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off." A decrease in activity is not followed by a decrease in appetite.

In women, there are three periods when they tend to gain weight:- (1) immediately after growth has stopped, (2) after child-bearing, and (3) at the menopause. All these ages are associated with the physiological alteration of the ovaries.

Race

Obesity is observed more frequently in certain races than in others. Joslin (56) points out that both obesity and diabetes are more common in the Jewish race. However, this factor may be explained on the different dietary habits rather than by any racial peculiarity. Natives of countries where the food supply is intermittent often store up a reserve of fat to live on when food supplies are low. Some tribes of Central Africa swing annually from the extreme of corpulence to excessive leanness. Uncle Sam, lean and gaunt, no longer typifies the American citizen who has assumed, as the result of prosperity, more John Bull-like proportions. The corpulent German of pre-war days had disappeared by 1918.

Race, however, is not the deciding factor in obesity. Environment and habit are much more important.

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Climate

Climate plays a part very similar to that played by race. It is a matter of environment. In the temperate zone most people lose weight in the summer and gain weight in the winter. This may be due to nature accommodating the body to external conditions; but, more likely, the warmth and quietness of indoor life during the winter months help to increase weight, while the outdoor exercise in warm months tends to lose a person's weight. Also, summer weather is not as likely to induce a hearty appetite as in winter weather.

Occupation

Christie (23) points out that the civilized life of today is a very unnatural one. The whole method of earning one's living has changed in recent years. This is an age of intensive industry; but it is mechanized. The fireman of the modern ship feeds his furnace by turning on the tap of an oil spray; whereas, his predecessor had to feed his boilers by shoveling coal. Labor in many factories is merely the controlling of an automatic device. Elevators have been installed in public buildings to save muscular effort. Brains have replaced brawn, but intellectual activity does not burn calories. An individual's occupation must be granted a large part in the production of corpulence.

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Attention is often called to brewers, inn-keepers, bakers, and butchers as examples of people who become fat because of great calorie intake. Silver and Bauer (103), however, were unable to establish any relationship between occupation and obesity. They say that if occupation were important as an etiological factor, all sedentary workers would be fat and all laborers thin. However, the clerk who is "nothing but skin and bones" is too well known to make it necessary to insist upon the lack of correlation between occupation and obesity. But, we must also consider the "starvation wages" of many clerks in this connection.

Sex

The relationship of sex to obesity has been discussed under the section on age. Dunlop and Murray (34) found that of 523 cases of obesity, 489 were females. Preble (93) in one thousand cases found 756 were females. Wilder (124) has an interesting theory regarding the higher incidence of obesity in females. "We may witness here to an adaptation for race survival acquired in the struggle for existence in the nebulous time of the beginning of homo sapiens when living conditions were precarious, and the young required the continuous presence of the mother. It may be presumed that the pithecanthropic male took the

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responsibilities of fatherhood relatively lightly, foraged mainly for himself and found his food with reasonable regularity. The female, on the other hand, was confined by her offspring to her cave and must have to endure long periods of fasting. The ability to store food as body fat was for her a singular asset, the utility of which many of her present day descendants are little prepared to appreciate."

Temperament

Graefe (45) points out the easy going nature of the obese person who is inclined not to be worried by his environment and who tends to avoid all excessive exercise. Christie (23) notes the phlegmatic personality of the obese with a tendency to spare muscular movements. The economy of effort practiced by the obese is apparent to all.

Newburgh (84) and Harrington (50), on the other hand, believe that this easy going personality has nothing to do with the development of obesity. Rather, the obese usually exhibit an emotional, nervous, highly excitable type of personality. These people obtain relief from nervous tension states by the nibbling of food much as others obtain relief by smoking. Harrington (50) cites the example of a girl who had lost weight by reducing but had gained it all back when she was thrust into the emotional

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stress and strain of nursing her mother through a serious illness. In the words of this patient, "I, sometimes, feel so nervous, I just have to eat."

Posture

Kerr (60) noted in studying the postures of seven hundred Harvard freshmen that there were four types of bodily posture.

Group A---7.5%---Head straight above chest, hips, and feet. Chest up and forward. Abdomen flat.

Group B--12.5%---Head too far forward. Chest not so well up and forward. Abdomen flat.

Group C--55.0%---Head forward. Chest flat. Abdomen relaxed and forward. Back curves exaggerated.

Group D--25.0%---Head still further forward on the chest. Chest still fatter. Abdomen completely relaxed. Back curves exaggerated to the extreme.

Young individuals of Groups D and C were prone to develop obesity especially of the abdomen later in middle life.

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Exogenous vs Endogenous Theories of Obesity

Obesity is always due to overfeeding; in this connection overfeeding stands for an excess of nutritional calories above the amount actually required. It does not matter whether the requirement is normal or increased. There is no sense in comparing the requirements of one individual with another. Each patient must be judged by his own standard. Von Noorden (116) first distinguished two types of obesity; those patients whose caloric intake was obviously greatly increased over their actual needs (these he called exogenous cases) and those patients who caloric intake was normal or even below normal, but who nevertheless became obese (these he called endogenous cases.)

Theory of Exogenous Obesity -- (Alimentary obesity, Nutritional Obesity.)

This theory says that obesity is due to a disturbance of the energy balance (energy intake over energy outgo) in the positive direction. The patient of this type becomes obese because he eats too much or exercises too little.

Theory of Endogenous Obesity -- (Metabolic obesity, Constitutional obesity, Endocrine obesity.)

This theory holds that obesity is in many cases primarily due to an altered metabolism of the individual so that

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he either has a decreased energy need, or is enabled to use his energy intake more economically. In this way his energy balance also become positive. The most popular method of explaining this endogenous type of obesity is on the basis of dysfunction of the endocrine glands. However, a great deal of investigation has been done on the metabolism of these individuals. Some investigations have also been carried out as to the heredity of these individuals as well as the lipophilia of the tissue cells themselves. All of these theories will be discussed later.

The purpose of this section of the paper is to weigh the evidence in favor of each of these two theories. Exogenous versus endogenous has been a hot bed of argument every since Von Noorden brought out this type of classification in 1910.

Newburgh (84) is the strongest advocate of the exogenous theory. He says that obesity is never directly caused by an abnormal metabolism, but is always due to a food ingestion that is greater than needed to replace the food consumption. Of course, everyone agrees that obesity is due to overingestion of food beyond the caloric needs of the body, but the question to be answered is why do these obese persons tend to overingestion in

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the first place? Newburgh (84) believes they overeat simply because they like to overeat. When the objection is raised that an adult individual will maintain a uniform weight never varying more than a pound for years in spite of wide fluctuations in consumption of food from day to day, Newburgh says that this fat regulatory mechanism depends upon the appetite. He believes that obesity is due to a dulling of the appetite stimulus, which prevents most of us from overeating, by persistent disregard of this stimulus. This question of appetite will be discussed more completely under a later section.

However, as Graefe (45) has pointed out, the fact that many persons become fat because they overeat, does not explain why they overeat. Might not the factors of overindulgence (love of food) and decreased activity (laziness) also be ascribed to the constitutional and endocrine make up of the individual. Hagedorn, Holten and Johansen (49) do not believe that obesity can always be due exclusively to overnutrition. There must be a regulation independent of appetite. Joslin (56) has pointed out the frequency of diabetes occurring in obese persons, and Hagedorn et al. think then that diabetes and obesity must have the same, or any a rate, a very similar disarrangement of metabolism as the underlying

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cause. They believe this abnormality was a tendency for an increased transformation of carbohydrate into fat. Joslin (56) himself also feels that because diabetes and obesity are so closely related, there must be a similar dysfunction in both.

Goldblatt, Smith, and Gardiner-Hill (43) carry this side of the argument a bit further. They believe that the only distinction, from the point of view of carbohydrate metabolism, which can be drawn between cases, grouped clinically and etiologically as exogenous and endogenous is that in the early stages of endogenous obesity, there exists a markedly increased carbohydrate tolerance in both storage and oxidation. In the intermediate and late stages of endogenous obesity, there is a tendency toward a more marked lack of tolerance to carbohydrate so that blood studies approach the condition seen in diabetes. They state,

"The point to be emphasized is that the difference between exogenous and endogenous types of obesity is only one of degree, not of kind, and that both are the result of disordered metabolism, which in the last analysis is due to glandular dysfunction."

Gusman (48) believes that all obesity at the onset is exogenous in nature, but with persistent overeating

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tends to become endogenous. He stresses the importance of the endocrine chain of glands in the control of the metabolic processes in the body. Because of the adaptive ability of this endocrine control, we are able occasionally to eat much more than our caloric requirement, e.g. Thanksgiving Day dinner, without any change in weight. However, if we continue to overeat as a regular thing, our endocrine mechanism becomes exhausted, and obesity develops. This is a very attractive theory, but still doesn't explain why we overeat in the first place.

Strouse and Dye (111) also believe that many cases of obesity cannot be explained purely on a nutritional basis. They report four cases of **obesity** that failed to lose weight over the period of one month, although they continued to work on a sub maintenance diet. Newburgh (84) has a ready answer for this argument. He

says that this failure to lose weight is due to water retention under the influence of the reduction diet. In a complicated set of calculations, he shows that the predicted weight loss from month to month, and even from day to day equals the actual weight loss, when exact observations are made on the fluid intake, fluid output and insensible perspiration.

Silver and Bauer (103) do not even believe that fat

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deposition is the result of positive energy balance. They postulate, rather, that certain tissues of the body have an inborn or constitutional tendency to store fat tissue. They believe that this inborn tendency becomes active under the effect of the endocrine glands. They point out that metabolism can have little to do with the development of obesity because hypothyroidism, Addison's disease, pluriglandular insufficiency, and hypophyseal cachexia all have a low metabolic rate, and yet are not all characterized by obesity. Graefe (45) says while this theory may be true, it cannot be considered as a primary factor. It is more important in explaining the distribution of the fat in the various tissues after the obesity develops. The pituitary hormones seem to have a special affinity for the cells below the waist line and the thyroid substance is most active above the waist. Roughly, the distribution of the fat in the hypothyroid is over the back and shoulders, while we are all familiar with the "girdle obesity" seen in hypopituitary states.

Barr (3), on the other hand, says that in spite of the popularity of ascribing hypertension, obesity, diabetes, and hypoglycemia to endocrine disturbance, the fact remains that the great majority of cases of

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these conditions display no clinical evidence of endocrine disease. He admits that an occasional case has been demonstrated associated with some anatomical pathology of the endocrine system, but repeats that these cases are rather rare. Some cases of endocrine dysfunction may be due to hyperplasia or hypoplasia, such conditions being very difficult to demonstrate. Hunter (53) believes that in the vast majority of cases in which no organic lesion can be found are due solely to over-ingestion of food stuff. Christie (23) sets the figure of 10% as the properpercentage of cases of obesity due to endocrine dysfunction in adult life.

Kern (29) in a series of 38 cases (unselected) found 78% of obese males and 74% of obese females had some endocrine dysfunction, and that in both sexes, the greatest percentage of these were associated with dysfunction of the thyroid gland. This last paper is quoted only to show the wide variation of reports as to the incidence of endocrine disorder. Newburgh says there are none, Kern says 76%.

Conclusions

In the opinion of this author, the question of exogenous and endogenous obesity is as unsettled as ever. As has been pointed out above, there are three

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main schools of thought:

1. Those who hold that obesity is entirely exogenous. (Newburgh (84)).
2. Those who maintain that obesity is entirely endogenous (Kern (59), Silver and Bauer (103), and Gusman (48)).
3. Those who maintain that both types occur.

The chief factors for postulating an endogenous type of obesity are the clinical observations, made so commonly that they cannot be entirely neglected.

- a. Frequent history of suddenness of weight gain, associated with other symptoms of dysfunction of some endocrine gland.
- b. Difficulty with which these patients lose weight on reduction diets.
- c. The frequent observations that many obese persons are really small eaters.
- d. The constant level at which the weight is maintained once the patient reaches a certain degree of obesity.
- e. Hereditary tendency.

On the other hand, the chief support for the exogenous theory is the fact that a tremendous amount of investigation on a laboratory basis has failed to re-

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veal any constant alteration in metabolism. As will be shown under the section on metabolism, most cases of obesity show a normal basal metabolic rate, no change in the specific dynamic action of their food, and no evidence of an increased efficiency in muscular action or increased economy in the metabolism of food.

Exogenous Obesity

As was described in the previous section, the theory of exogenous obesity holds that the deposit of excess calories as fat is due entirely to overingestion of calories. For the purposes of discussion, this definition of exogenous will be broadened so that all cases of obesity which do not show evidence of endocrine disease (lowered basal metabolic rate, change in sexual characteristics, etc.) will be included.

The incidence of exogenous obesity has been well stated by Christie (23). He gives the following periods in the life cycle when exogenous obesity is the most common.

a. Infants--obesity seen in infants is almost always exogenous in origin. It is more common in bottle fed babies, in which the formula used is too rich, especially in carbohydrate. However it sometimes occurs even in breast fed infants. Some mothers seem endowed

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with a richer quality of milk than normal. Christie says that a few cases of infantile obesity are due to a hypothyroid state (cretinism). This condition must always be excluded in the differential diagnosis.

b. Children--exogenous obesity is almost never seen in children. Like all young animals, they consume too much energy growing and in excess activity. Obesity in children most commonly occurs at the time of puberty and is almost always due to pituitary or thyro-pituitary insufficiency.

c. Adults.--Ninety percent of the obesity seen in adults is exogenous. In men, the onset of obesity is most common after forty years of age, when the individual has attained a fair amount of prosperity. Women are most prone to obese after pregnancy. According to Christie, this may occur because of an increased appetite developed during pregnancy, but may likewise be due to a temporary endocrine imbalance. Also, many young women tend to become somewhat obese as they reach the end of the growth period. This is also endocrine in nature.

In any attempt to explain the so called "simple" type of obesity, the question immediately arises, -- Why does the energy balance become positive and force

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the development of obesity? Most people tend to overeat, yet only a comparatively small percentage of the population becomes obese. What happens in certain individuals that they become obese? Excluding the small percentage of cases due to endocrine dysfunction, there are three main schools of thought regarding these questions; the first, that maintain there is some change in the appetite mechanism, the second, that believe that there is also some constitutional or heredity feature, and the third, that holds there is some change in the combustion processes in the body.

Appetite

Newburgh (84) is the great champion of the exogenous theory of obesity. After prolonged and careful studies on the obese and normal patients in a "metabolic cage", measuring carefully the amount of food given, the weight loss both obvious and insensible and checking the metabolic rates, he concluded that obesity is always exogenous. It is due to persistent overeating and dulling of the appetite stimulus. Newburgh believes, in contrast to the popular opinion that the fat person is slow moving, good natured individual, that the obese person almost always exhibits an emotional, unstable personality. He obtains relief of nervous tension states by the re-

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peated nibbling of food.

Harrington (50) working in Newburgh's laboratory, studied this mechanism of the appetite in some detail. She found, in the study of three normal individuals, that all three gained weight on a concentrated diet, and lost weight on a bulky diet. These persons were allowed to eat as much as they wanted to, only the quality of the diet being changed. She concluded that gastric distention had very little to do with appetite, but that taste did. All three individuals admitted that they ate a larger quantity of the concentrated diet because of the sweeter taste. She also believes that obese persons eat to relieve nervous tension states, e g. women at bridge parties nibble at candy instead of reaching for a cigarette. Many individuals attend after theater parties, not because they are hungry, but to have something to do. She quotes the case of one girl who desired to lose weight in order to obtain a job as a private secretary. She lost considerable weight on a reduction diet. When she was married sometime later, she gained back all the weight she had previously lost during her honeymoon. She reported that it was impossible to select her diets carefully in hotels.

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Cheny (22) draws a distinction between hunger and appetite stimulation. Hunger is an unpleasant sensation which occurs when the stomach is empty and is due to gastric contractions. It varies from a hollow feeling to a gnawing pain in the epigastrium. Appetite, on the other hand, is a desire for a particular food or drink which is a pleasure, and depends on previous acquaintance with the substance in question. It occurs before appointed meal times or may be aroused by the taste or smell of food. Thus hunger is an organic stimulation, while appetite is a psychic stimulation. In the obese, appetite may increase so much that it represents a mild form of psychoneurosis.

Graefe (45) stresses the importance of appetite and the feeling of satiety in limiting the caloric intake. The feeling of satiety is a complex mechanism and certainly does not set in with the rapidity of a reflex. It needs time to develop. This regulatory principle suffers under abnormal conditions. He shows that in Germany in the post war period, there was a rapid increase in the incidence of obesity. Foodstuffs which the Germans had had to deny themselves for years were available again in increasing amounts. The mechanism which had been practically out of use for so long no

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longer functioned accurately. There followed a reinstated almost physiological hyperappetite. The joy, so long denied, of eating one's fill, kept the voice of satiety from sounding the warning in time or at all. The result was a rapid increase in obesity from 1924 to 1926.

Familiar to all, is the rapid gain of weight, sometimes far above normal, in convalescents, who have suffered from a long devastating disease. There are some cases in which increased appetite amounts to a compulsion neurosis. Graefe (45) quotes, in his textbook, an exaggerated example of hyperappetite from C.F. Graefe, early in the nineteenth century.

"Early in this thirtieth year, the patient's appetite became so enormous that he was obliged to eat twelve pounds of meat besides the rest of his meals during the day. If there was a bet upon it, he was able to eat a whole calf at one sitting without apparent discomfort. That there was no disturbance causing this condition is evident from the fact that under proper medical treatment, his weight dropped from 363 to 209 pounds in eight months."

Christie (23) says that this hyperappetite is seldom the result of over indulgence in an excess amount of foodstuff. Rather, the majority of the obese are gourmets

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in that they indulge in the flavor of certain fat forming foods. Some individuals are carbohydrate eaters (potatoes, bread, cakes, whiskey). Others are attracted by fats (butter, cream, cheese), while the tooth of the third is definitely "sweet."

Strang and McClugage (109) in studying the specific dynamic action of food in obese patients, found that there was no significant difference in the amount of heat production increase in the obese, normal, and thin groups. However they did observe that the rate of heat production was slower in the obese; the obese group did show maximum heat production until the second hour after a mixed meal, while the thin and normal groups showed the maximum heat production in the first hour. They concluded that satiety occurred sooner in the thin person because he "gets hot" faster. He avoids further eating to avoid discomfort of further overheating. The obese person eats more because he has more time before uncomfortable overheating occurs. While this observation is interesting, it does not explain why a person gets fat in the first place. If the normal person has a rapid rate of heat production, why does he ever overeat, and allow himself to become fat and develop this slow rate of heat production? Evans (36) agrees with this theory,

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but believes that the obesity, at first, is a habit of overeating, the overeating being primary. Later when obesity is well established, the slower rate of overheating becomes established and the obesity becomes secondary to it, thus forming a vicious cycle. The only objection to this type of reasoning is the common clinical observation that fat persons do not tend to increase in weight once they have reached a certain level of overweightness. This usually happens within the first five years of the obese condition. If this vicious cycle theory is right, one would expect the obese person to continue to gain in weight.

Lambie (65) points out the frequency with which college athletes "swallow their footballs." He believes that appetite habits are set at one level of energy output and persist in spite of a lowered energy level. The basal metabolic rate declines slowly after 35 years of age. The persistence of food habits may account for the increasing incidence of obesity after forty years of age.

Many authors have pointed out the dependence of hunger stimuli on the level of the sugar in the blood. This blood sugar level depends on insulin secretion. These authors believe that increased insulin secretion

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results in a fall of blood sugar giving rise to an increased hunger stimulation. If this is a persistent process, it may result in obesity. This theory will be discussed in detail later under the section on Endocrine obesity.

Heredity

In contrast to the idea that exogenous obesity is due solely to hyperalimentation because of acquired faulty food habits, etc., many authors say that there must be another factor which is at least coincident with if not the cause of the increased appetite. The constitutional theory of obesity depends on this concept. The constitutional theory holds that "simple" obesity is not simple at all but is closely related to the constitutional and endocrine patterns of the individual.

Davenport (26) observed that two slender parents rarely have a fleshy child, and that most of the children of obese parents tend to obesity. The union of one slender parent and one fleshy parent usually results in fleshy children, but not as markedly so as when both parents are fleshy. These observations are suggestive that obesity should be considered an inherited characteristic, and probably a dominant one at that. Davenport observed that as children grow older, they tend to undergo the same changes in regard to weight and height as

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their parents did. From these observations, Davenport states that in the population at large, there are three biological types: slender, medium, and fleshy. Most individuals fall into one of these three types. There are very few individuals that are intermediate between these three.

Carrying these observations further, Davenport and Nelson (27) applied statistical methods to 402 persons from 71 families. They measured the chest girth as a standard of nutritional state (undernourished children have a small skeletal frame, while those well nourished from infancy have a large skeletal frame well covered with muscle and fat.) Then they graded the appetite and the degree of activity by questioning both the subject and members of the families of the subjects. By their calculations, they attempted to correlate the observed nutritional state with the degree of activity and the appetite as reported to them. They found no correlation at all among these factors. Then they concluded that body build must be a constitutional phenomenon: endocrine idiosyncracies and metabolic peculiarities may be inherited.

Joslin (56) also observed the frequency of diabetes in the Jewish race. He stresses the high incidence of

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diabetes in the obese individuals. In 1000 cases of diabetes, 77% were obese. He points out the fact that the Jewish race as a whole are prone to be heavy eaters.

Gurney (47) analysed 75 cases of stout women and 57 cases of non stout women between 20 and 50 years of life. In comparing the history of these two groups as to the stoutness of their parents, he drew up the following table::

Group	Mother Stout	Mother and Father Stout	Father Stout	Mother and Father Non Stout
Stout Women	43%	25%	15%	18%
Non Stout Women	30%	6%	0.5%	62%

Analysis of these cases on the basis of the progeny obtained from the stout and non stout parents, he found the following:

Matings	Stout Progeny	Non Stout Progeny
Stout x Stout	73%	27%
Stout x Non Stout	41%	59%
Non Stout x Non Stout	9%	91%

Gurney concluded that stout parents have a gamete for slenderness and non stout parents rarely have a gamete for stoutness. Because of this, regression to a more normal build, as a result of these gametes for slenderness in the obese partents, can be seen in the offspring of stout parents to a considerable greater degree than in the offspring of slender parents toward obesity.

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Rony (95) also thought that heredity must be very important in body weight. He says that obese, normal and lean persons revert to their previous weight when treatment stops. This indicates that there is a delicate and sensitive mechanism regulating the fat content of the body in all persons. This mechanism, which may be compared to the body heat or water volume regulating mechanisms, is governed by the existing fat content of the body for the person's age, sex, and height. In the normal person, when the fat content rises, this mechanism causes a decreased appetite and an increased activity and possibly an increased specific dynamic action of food. This restores the normal fat content of the body. This mechanism is set a certain level genetically but may be influenced or changed by hormonal (endocrine obesity) or nervous (Dercum's disease) influences. In obesity, this mechanism is set abnormally high, and in lean persons, it is set abnormally low. However, its operation is no less efficient than in the normal person, as evidenced by the rapidity with which an obese person will regain his weight when he goes off his reduction diet.

Newburgh (84), however, says that heredity is of no importance in obesity. He suggest rather that obese

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parents, who have acquired the habit of overeating, train their children to overeat also. Joslin (56) admits this possibility.

A modification of the hereditary theory is stated by Silver and Bauer (103). These authors claim that there is a lipophilia of the tissues so that they tend to store fat. Certain tissues tend to store fat more readily than other tissues, e.g. the abdominal wall. Silver and Bauer believe that in the obese, this tendency is more marked in these regions and also active in other regions where it is not normally present. They state that this lipophilia should be regarded as a hereditary tendency, although, like many congenital traits, may not become active for many years after birth. v. Bergman (115) also propounded this theory of lipomatous tendency. He described it as a condition of abnormally facilitated fat production and impeded fat destruction. He claims that obesity in some cases is sort of a lipomatosis universalis in the sense that the lipophilia in a certain tissue is primary, and the sparing in the energy expended is secondary.

Metabolism

The other popular answer to the question asking why certain individuals tend to become fat presupposes some

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some disorder in the metabolism of the individual as the primary cause. They believe that obesity depends not so much on an increased energy intake as a decreased energy output. A tremendous amount of research, and a tremendous amount of pure philosophy appear in the literature regarding this subject. The difficulty in establishing an altered metabolism as the primary cause of obesity is that the metabolic tests are applied to individuals who have already become obese. It is impossible to say then whether the obesity is the result of the changed metabolism or the changed metabolism is the result of the obesity. Many authors recognize this difficulty and say that metabolic determinations should be carried out so that not the observed surface area, but the ideal surface area if the patient were of normal size and shape for his sex and age is used as the basis for calculations. The results of this vast amount of investigation have been more confusing than helpful. As in quoting scriptures, any person with sufficient "scientific or clinical prestige" can set up a theory as to the cause of obesity and find plenty of results in the literature to support him. For example, the famous Dr. X. can postulate a lowered basal metabolic rate in obesity and support it with a voluminous bibliography, as long as he

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is careful not to mention an equally large series of authors who report a normal or even elevated basal metabolic rate in obesity, not to mention those who claim that even the lowered basal metabolic rates are in reality even elevated when recalculated on the basis of ideal surface area.

The purpose of this paper is not to take sides with any one particular theory of obesity, but to report in some detail all the commoner theories and the reader himself may be the judge. The commoner theories regarding this altered metabolism will be listed below. The reader is referred to the section on metabolism for detailed discussion pro and con for each theory.

1. A decreased basal metabolic rate--the early workers in metabolism reported a very high incidence of cases of obesity with a decreased metabolic rate. They of course postulated this as the most common cause of obesity. However with the establishment of better standards and from the report of a great many determinations on the metabolism in thin, normal, and obese groups, it was found that the distribution of the obese into high, low, and normal metabolic rates was so inconstant and irregular as to be of no use in determining the etiology of the condition.

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2. A decreased total metabolism--some authors believe that basal metabolism determinations are not indicative of the total metabolism, and that obesity is the result in a decreased total metabolism, not a decrease in the basal metabolism. Bernhardt (11) is a good example of this group. He believes that during the twenty-four hour period, there are times when the metabolic rate is depressed somewhat below the basal metabolic rate as determined in the morning. He called these negative phases, and said they were most prone to occur after light exercise, taking food, and during sleep. Unfortunately, other authors have been unable to confirm this.

3. Muscular economy--some authors report that obese persons are able to perform muscular exercise more efficiently than normal individuals, and that they consequently require less energy. Other investigators report just the opposite. Common observation of the inefficiency of the fat person in any atheletic competition would tend to discard this theory.

4. Food economy--the supporters of this theory hold that the obese person is able to extract a larger number of calories from a given amount of food ingested than the normal person can. The usual mechanism given

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is that the specific dynamic effect of the food, especially protein, is decreased in the obese, giving him a larger supply of calories. So many authors, including Rolly (94), Wang, Strouse, and Saunders (118), Plaut (91), Mason (74), and Bernhardt (11), have reported this decrease in the obese group that it cannot be disregarded. However, this action decrease amounts to only 1 to 5%, and this amount does not seem sufficient to account for a very substantial gain in weight.

5. Altered combustion mechanism--This theory holds that the obese have a qualitative type of metabolism change. Most authors report a lower respiratory quotient in the obese, indicating that they are burning a different type of mixture than the normal. The interpretation of this varies considerably. Many men feel that this low R.Q. indicates an increased tendency to store carbohydrate as fat. On the other hand, one might think that the lowered R.Q. is the result of, not the cause of obesity. The obese person has a lower respiratory quotient simply because he has a greater proportion of fat tissue to burn than the normal person.

6. Luxus consumption--because of the frequent demonstration of a drop in the basal metabolic rate as the result of starvation, Graefe (46) felt that there

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must also be a compensatory rise in basal metabolism as the result of persistent overfeeding. Others, again, have been unable to demonstrate this as well as Graefe did. This theory cannot be accepted, therefore, until further proof is offered.

7. Water retention--many authors have pointed out that much of the increased body weight in some cases of obesity was not due to fat deposition alone, but was also due to water retention. The most modern thought regarding this matter, as expressed by Newburgh and Johnston (85), is that water retention is slight in fat tissue until the energy balance is upset at the onset of a reduction diet.

8. Increased carbohydrate tolerance--this theory holds that the obese individual has a peculiar ability to burn glucose with a marked thoroughness, and thus spares his protein and fat tissues. This theory is based on the observation that many obese persons have an increased glucose tolerance curve as indicated by blood chemistry methods. This theory is tied up with pancreatic function and will be discussed under the section on endocrine obesity. Ogilvie (87) says that during the first five years of obesity, at least 50% of the cases show an increased tolerance.

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Endocrine Obesity

Endocrine obesity may be defined as obesity associated with some pathology of one or more of the endocrine glands and characterized by obesity of rapid onset, characteristic fat distribution, resistance to treatment, and associated with other symptoms and signs of the various endocrine complexes. Endocrine obesity has been very popular, at least with the lay public, because it offers a water tight excuse for being overweight. To the physicians, it has not proved so popular, however, because of the difficulty and expense of differential diagnosis and the remarkable resistance of these patients to any form of reduction therapy. Substitution therapy with the various endocrine preparations has, even with a careful and accurate differential diagnosis, at best proved to be a prolonged trial and error proposition.

Classification

Endocrine obesity has been classified according to age by Christie (23), Engelbach (35) and Tidy (113). Engelbach, for example says that there are three different types according to age:

1. Infantile type--hypothyroidism (cretinism.)
2. Juvenile type--hypopituitarism (Fröhlich's

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syndrome) and hypopituitary-hypothyroidism.

3. Adult type--hypogonadism (after 35 years.)

Many authors, for instance Weber (123) have advocated the classification according to the distribution of the fat, e.g. the girdle obesity of pituitary origin, the upper extremity obesity of thyroid origin, and the trochanteric obesity of gonad origin. Graefe (45) says that this division is illogical except for a very small percentage of typical, sharply defined forms. In at least 80% of the cases, fat distribution gives no indication as to the origin of the obesity.

The purpose of this section of the paper is to describe the various endocrine types of obesity. The relationship of exogenous and endogenous obesity has been discussed in a previous section of the etiology. (See Exogenous vs Endogenous.) Although there is no good distinction between exogenous and endogenous obesity, and also in spite of the fact that the various types in the endocrine group itself are not clearly differentiated, we will discuss each type independently as though it were a clinical entity with no relationship to the others. Also, the obesities due to damage to the higher nervous centers will be discussed independently in spite of their close relationship to

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pituitary obesity.

Pituitary Gland

In 1898, Fröhlich (39) first described the condition later to be called dystrophia adiposogenitalis or Fröhlich's Syndrome. His patient was that of a boy, fourteen years of age, who had suffered two years with headache and vomiting, and had gained weight rapidly. The fat distribution was about the girdle region. The genitalia were underdeveloped, and the pubic and axillary hair were absent. Since that time various types of obesity have been ascribed to pituitary origin, but only two have stood the test of time, Fröhlich's syndrome and Cushing's pituitary basophilism. There are several types of Fröhlich's syndrome. Lissner (67) says that all cases of pituitary obesity should be called Fröhlich's syndrome and classified as follows:

a. Childhood types

1. Lorrain type with skeletal undergrowth
2. Brissaud type with normal skeletal growth

b. Adolescent type--original Fröhlich type

c. Adult type

d. Hypopituitarism with acromegaly (Cushing type)

e. Adiposis dolorosa (Dercum's disease)

f. Dystrophia adiposogenitalis with atypical retinitis pigmentosa and mental deficiency (Lawrence-Biedel Syndrome)

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In this paper, we will discuss Fröhlich's syndrome with its variations as one entity, and Cushing's type as another entity. Dercum's disease will be considered later under the section of nervous obesities.

a. Fröhlich's Syndrome (Adiposogenitalis)

This condition may be defined as a syndrome complex due to underfunction of the hypophysis, characterized by obesity, genital hypoplasia, and faulty skeletal development, associated with nervous and mental symptoms which are either the direct result of deficient secretion or dependent upon local or general intracranial pressure. (Definition by Beck (5)). The classical type of adiposogenitalis described by Fröhlich occurred in an adolescent boy with the onset at the time of puberty. This is the most common type of pituitary obesity, and also the most frequent type seen during adolescence. Loewenberg (68) describes the various types of Fröhlich's syndrome, thus:

1. Lorrain type--occurs before puberty. The patient is small in stature and delicately formed. The face is characterized by fine features. There is no obesity. The only excess fat occurs over the mons veneris. The legs are long and slender. The genitals are small and secondary sex characteristics are absent. The mentality is bright.

2. Brissaud's type--occurs before puberty. The skeleton is underdeveloped. The neck is short and stubby. The body is covered by a thick layer of fat which is universal in character. The face

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has a characteristic "pudding face" appearance. There are no secondary sexual characteristics developed. The mentality is dull. Torpidity and somnolence is common. The carbohydrate tolerance is usually elevated. Tidy (113) suggests that the Fat Boy in "Pickwick" was such an individual.

3. Adolescent type--this type occurs about the time of puberty. The skeletal growth is retarded so the individual becomes short and stocky. Obesity develops rapidly and tends to assume a fairly definite type of distribution with relative increase of subcutaneous deposits about the hips, thighs, mons, and lower abdomen - the so called "girdle obesity." The fingers tend to be tapering. There is genital dystrophy in both sexes. The penis is rudimentary and is often almost hidden in cushions of fat. The prostate and scrotum remain small. The pubic hair has a feminine type of distribution. In the female, the clitoris is short, and the labia minora are small. The uterus retains its infantile shape and size. The ovaries are usually not palpable. Both menstruation and ovulation are usually absent. The carbohydrate tolerance is high. There is a low blood pressure and subnormal temperature. The basal metabolic rate is usually subnormal.

4 Late adult type--occurs near the menopause. The patient puts on weight rapidly of the girdle type. The dystrophy of the sexual organs and the loss of libido is not marked. Rather the patient complains of pressure symptoms (headache, hemianopsia, epilepsy.)

5. Associated with Acromegaly.--In these patient's there is a long history of acromegaly (due to hyperpituitarism), but after many years, the patient becomes fat, presents the symptoms of hypopituitarism.

6. Associated with atypical retinitis pigmentosa and mental deficiency--Lawrence-Biedel Syndrome. This disturbance is characterized by all the symptoms of Fröhlich's Syndrome plus mental deficiency. Examination of the eyes shows the retinitis. This is a congenital disease, and is usually seen in several members of the same family. Often other congenital defects are present.

The development of this syndrome is caused by hypo-

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secretion of the pituitary gland. The reason for the hyposecretion is difficult to explain because many cases show little or no gross or microscopic pathology of the pituitary gland. Christie (23) said the etiology of this condition was fourfold:

- a. Congenital or primary hypoplasia
- b. Traumatic--skull fracture
- c. Inflammatory--tuberculosis, toxins from infectious diseases
- d. Pressure--tumors developing in this neighborhood, e.g. craniopharyngioma

Beck (5) lists the same four causes but stresses in particular the prescence of tumor in or near the hypophysis. Masterman-Woods (76) said the only cause of this disease was insufficiency of the posterior pituitary hormone. Kern (59) recognizes the syndrome but says that he doesn't know whether it is posterior, anterior, or intermediate pituitary or a combination. Meagher and Heuer (80) say that the syndrome may be due either to craniopharyngioma or to chromophil adenoma of the anterior pituitary. Mazer and Goldstein (78) suggest that the condition might be due to a concomittant involvement of the pituitary gland and the tuber cinereum. Loewenberg (68) says that sometimes the condition may be due

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entirely to involvement of the tuber cinereum or hypothalamus.

Probably Mazer and Goldstein(78) come nearest the truth. The symptoms of genital dystrophy and skeletal undergrowth depend on crowding out of the chromophil cells of the anterior pituitary. The symptoms of somnolence, retinitis, mental deficiency depend on the pressure on the hypothalamus and cerebrum. Headache depends on increased intracranial pressure, while blindness results from pressure on the optic chiasma. The obesity itself may be due to a pituitary lesion, or may be due to interference with a possible fat center in or near the tuber cinereum. This question will be discussed later under the nervous theory of obesity.

b. Cushing's Syndrome--(Pituitary Basophilism)

Cushing (25) defines his syndrome as due to an atypical pituitary tumor and characterized by a rapidly acquired adiposity chiefly affecting the head, neck and trunk, sparing the extremities, leaving them strikingly thin looking. This adiposity has a peculiar tense more or less painful character. The individuals affected have a plethoric appearance. There is an exaggeration of secondary sex manifestations most often evidenced by an overgrowth of hair on the face and neck.

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The abdomen is often covered by purplish cutaneous striae. In the females, only very rare cases have been reported in males, there is an amenorrhea. There is a marked tendency to hypertension. Glycosuria is a frequent associated symptom. The red blood count and the hemoglobin percentage is often elevated. In the males there is a loss of libido with testicular atrophy. Softening of the bones with diminution in height and spinal kyphosis is common.

Regarding the nature of this syndrome, Cushing says that it is definitely a polyglandular disease with a pituitary origin. The gain in weight and the exaggeration of secondary sexual characteristics are pituitary in origin. The hypertension, hirsutism are due to dysfunction of the adrenal gland. The osteoporosis of the skeleton is probably parathyroid in origin. The pathology in the pituitary gland is usually not obvious. Microscopic study of serial sections is sometimes needed to demonstrate the very small adenomata of basophilic cells.

c. Posterior Pituitary.

Although posterior pituitary insufficiency has been pretty well ruled out as the cause of Fröhlich's syndrome, Rowntree and Brunsting (99) suggest it as a

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new possibility in the etiology of obesity. They quote the histories of two young women suffering from obesity associated with some pituitary symptoms. Both of these patients failed to lose weight on a reduction diet until they were also put on dehydration therapy. These authors suggested that the obesity in these cases was due to hyperactivity of prolactin A causing early puberty, with secondary hyperactivity of the posterior lobe resulting in retention of water; either by pitressin or the water hormone of Kamm. This condition would be the antithesis of diabetes insipidus.

Thyroid Gland

In his original classification of obesity, von Noorden (116) divided all cases into exogenous and endogenous. He said that the endogenous cases were due to a "hypothyroid state." Further investigation has failed to bear out von Noorden's conclusion that all cases of endogenous obesity were due to hypofunction of the thyroid.

According to Engelbach (35), the clinical picture of hypothyroid obesity is as follows:

"A smooth universal distribution of subdermal infiltration with cervical fat pads in the supraclavicular region and padding of the hands and feet on their dorsal surfaces. The face is full, 'moon-

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faced.' The trunk is uniformly covered with an even layer of adipose tissue. The extremities are obese to the finger tips."

Masterman-Woods (76) also describes this condition:

"The distribution of the fat is generalized with peculiarly marked focal excesses. These excesses are obvious in conformation of the face with its swollen lips and cheeks, puffy eyelids, underhanging secondary chins and immensely thickened neck. The supraclavicular hollows are completely obliterated. Upon both supra-scapular regions are large prominences. The arms are gross and the fingers and backs of the hands are puffy. The breasts and the abdomen are very fat, while the elephantine legs terminate in feet and toes swollen and puffy on their dorsal aspects."

In order to make a diagnosis of thyroidal obesity, however, the other symptoms (coarse dry hair, thickened skin, slow heart, lassitude, low B.M.R., increased blood cholesterol, and decreased sugar tolerance) must be present, at least in part. A low basal metabolic rate is not pathognomonic of thyroidal disease, because the B.M.R. may also be decreased in pituitary disease. The clinical descriptions given above are very similar to myxedema. This brings us the questions of just what are the differences between myxedema and obesity? Graefe (45) says that there is no difference, and that the term myxedema is an incorrect one. The change in the subcutaneous connective tissue is the result of physiochemical changes. For that matter, then obesity

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is also an incorrect term for this type of infiltration. Probably the gain in weight is only a symptom of thyroid disease and should not be confused with the gain in weight seen in obesity.

Several authors have suggested that the obesity is primary to the development of the hypothyroid state, instead of the opposite as suggested by von Noorden. Poulton (92) says that as a person gains weight, the same mass of active tissue, (muscles and glands) have to maintain a consequently higher rate of metabolism to keep up to the larger tissue mass. After a time, the thyroid gland tends to become insufficient from this overwork, much as a heart decompensates. Therefore, he reasons that the obese person is first a hyperthyroid, later a hypothyroid. Regarding the high blood cholesterol that is associated with hypothyroid states, Bruger and Poindexter (17) have shown that a high caloric diet, presumably high in carbohydrates and fats, which results in obesity is not accompanied by a rise of the plasma cholesterol in human beings. This would also tend to indicate that obesity must precede the hypothyroid state.

On the other hand, assuming that Graefe and Graham's (46) theory of luxus consumption is correct, the thyroid

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gland must be very important in the development of obesity because he showed that his dogs did not have any luxur consumption after the thyroid gland had been removed. Graefe felt that this was a very important fact and served as a bridge between endogenous and exogenous obesity.

It seems to this writer that the point at issue is the definition of the word obesity. If obesity means an increase in weight beyond the normal, then indeed the hypothyroid individual may be considered obese. However if obesity is limited only to those cases showing deposition of excess calories as normal fat, then hypothyroid has nothing to do with obesity. Myxedema and fat may not be considered the same substances.

Adrenal Glands

Unlike the other endocrine glands where hypofunction seems to cause obesity, hyperfunction of the cortex of the adrenal gland results in obesity in the female. Excess cortical hormone has no effect on the male after the time of puberty, but causes precocious development before that time. In the female, Cecil (21) describes the syndrome as follows:

Female children before puberty--"These children become fat. Seldom is there unusually muscular development as seen in boys. Hair appears early on the pubis and occasionally on the face. The skin

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becomes red, coarse, and dry. Acne is common. The voice becomes coarse and ugly. The clitoris assumes the shape of the penis. Menstruation does not start at puberty."

Females after puberty--"Usually the first symptom is cessation of menses. Normal sexual desire is decreased and sometimes is perverted to homosexuality. Hirsutism appears shortly after cessation of menses. The pubic hair is transformed to the male type, and hair begins to grow on the face. Later legs, arms, abdomen, chest, and back become covered with hair. The skin becomes red or brown and dry. Acne is common. The voice becomes masculine. The clitoris enlarges greatly, resembling the adult penis. The labia enlarge. The breasts atrophy. Obesity is one of the most striking symptoms. The distribution of fat is on the abdomen, chest, buttocks and hips. There is little if any fat deposited on the legs or arms. The face is full and unsightly owing to deposits of fat in the cheeks, under the chin and in the neck. Hypertension is observed in many of these patients."

The action of cortical hormone was first shown by Goldzieher (44). He showed that injection of cortical hormone in twenty-three rabbits over a prolonged period resulted in obesity. The immediate effect of the injection was a drop in the blood cholesterol. Goldzieher felt that this drop in blood cholesterol was brought about by the endothelial cells with a subsequent storage and fixation of the lipoids in the tissues.

By this and other work, the association of the hyperfunction of the cortex of the suprarenal gland and obesity seems well established. Packard and Wechsler (88) showed that patients suffering from suprarenal insufficiency gained weight rapidly on cortical hormone preparations. Koster, Goldzieher, Collens, and Victor (62)

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report a case that reduced from 330 pounds to 146 pounds inside of seven months following the removal of one adrenal gland, the cortex of which showed marked hyperplasia. Walters, Wilder, and Kepler (117) found an adenocarcinoma in the cortex of the adrenal gland in two cases at autopsy presenting typical adrenal symptom complexes. Another of their cases showed a benign adenoma of the cortex on operation.

The question, then is not whether excess cortical hormone causes obesity, but rather how this action is carried out? The work of Goldzieher (44), quoted above, would seem to indicate that this surplus cortin had a direct action on the endothelial cells of the body. However, Cushing (25) points out that there is very little difference between the above clinical syndrome and his own description of pituitary basophilism. He says that in fourteen cases showing corticoadrenal tumors, ten showed also a pituitary basophilic adenoma, when careful search was made for them by serial section. Walters, Wilder, and Kepler (117) however report only one case of ten which also showed a basophilic adenoma of the pituitary. Cecil (21) believes that the mechanism must in some way be connected with the gonads because cortical adenomata have no effect in males after

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puberty, or in females after the menopause. Insufficient evidence has been accumulated to determine whether or not this is a pluriglandular disease.

Gonads

The association of obesity with hypofunction of the gonads has been known since antiquity. One has only to refer to the eunuchoids or mention the ancient science of animal husbandry to prove this. In the adult, cases of endogenous obesity are due in a high percentage to gonadal dysfunction. Many obese women give pregnancy as the onset of their obesity. Masterman-Woods (71) describes the distribution of the obesity in these cases as trochanteric, as follows:

"In uncomplicated cases of hypogonadism, the panniculus adiposus is confined to the iliac crest, mons, upper and outer third of the thigh. This includes the area extending from just below the lateral margin of the iliac crest to an approximately equivalent distance below the greater trochanter, with its peak opposite the later bony prominence. The lower abdomen is also a favorite site. Sometimes there is fat deposited on the outer ends of the upper eyelids."

Apperman (1) points out that hypogonadism does not cause obesity in the adolescent or young adult. He says there are two kinds of eunuchoids; the tall type and the fat type. Many cases of obesity in the adolescent period are blamed on hypogonadism, when in reality they should be classified as Fröhlich's syndrome with secondary

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dystrophy of the gonads. Apperman says that the chief causes of hypogonadism in the male are malignancy, operation, congenital anomalies such as cryptorchidism, inflammations such as syphilis, gonorrhea, mumps, and secondary to other endocrine dysfunction as in adiposogenitalis.

The etiology of hypogonadism in the female, according to Mazier and Goldstein (78) are menopause, operation and secondary to other endocrine disorders, e.g. hypo or hyperthyroid, hypopituitary, and insufficiency of the medulla of the adrenal gland. Kern (59) has a rather novel theory of obesity in young women, saying,

"It is very probable that a good deal of the obesity seen in young women at the present time is possibly connected with restricted childbearing. Suppression of the natural function of reproduction and non use of the female resources for the bearing and nourishment of the fetus must be reflected in the release into the organism of fluids and energies which can be utilized only in the building of new tissue and adiposity."

Ogilvie (87) observed that in six cases of hypofunction of the ovaries (three postoperative, one primary hypoplasia, and two following repeated pregnancies,) there was a decreased glucose tolerance in all cases.

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He suggested that this might contribute to the development of obesity in these cases. However he did not check his observations on a similar non-obese group.

Pancreas

The fact that obesity might occur as the result of dysfunction of the pancreas has never been definitely established, but many authors have suggested some possible connection. For one thing, unlike the other glands, the obesity does not seem to have a characteristic distribution. Therefore, dysfunction of this gland has been postulated as a explanation for the mechanism in exogenous obesity. The glucose tolerance curve, like the basal metabolic rate in thyroid disease, has become the standard for measuring pancreatic function, although, again like the B.M.R., there is a similar alteration in many pituitary lesions.

Joslin (56) was the first to suggest some possible relationship of the pancreas with obesity because of the frequency with which diabetic patients had a history of of obesity. As Joslin puts it,

"Diabetes is the penalty of obesity."

In the analysis of 1000 of his diabetic cases, Joslin found that 77% were obese. Many workers have reported that in a certain percentage of cases, there is

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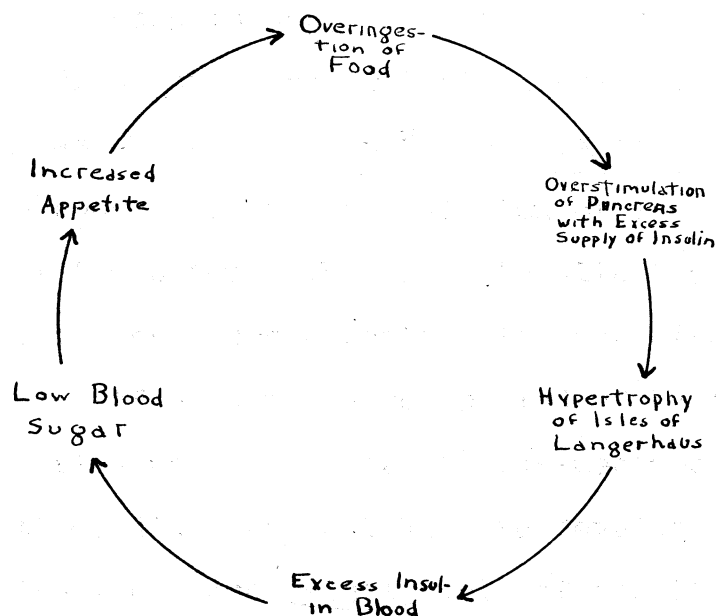
a decreased tolerance to glucose, the so called prediabetic type of curve. Paullin and Sauls (89) cite fifteen of twenty-eight cases of obesity which had such a prediabetic curve. Spriggs and Leigh (105) report on one hundred cases of obesity in which 57% had a normal tolerance, 20% had an increased tolerance, and 23% had a decreased tolerance. John (55) studied twelve cases and found that four of them had a prediabetic or diabetic type of glucose tolerance curve. Rony and Levy (98) found that in seventy cases, forty-four had a normal, sixteen had a low, and ten had a high tolerance for glucose. Roughly these figures average about 60% of the cases of obesity have a normal glucose tolerance curve, 20% have a depressed curve, and 20% have an elevated curve.

From these observations, several theories as to the origin of obesity have been proposed. John (55) says that the pancreas must be considered among the endocrine glands, the dysfunction of any of which may be responsible for obesity of the endogenous type. Hagedorn, Holten, and Johansen (49) also feel that the relationship of diabetes and obesity represents variations of the same process. However they feel that it is a tendency of the tissues themselves to convert

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carbohydrate into fat with little connection with the pancreas (See section on Metabolism, respiratory quotient.)

Poulton (92) says that the pancreas must have some role in the etiology of obesity because of the frequency that diabetes occurs in the obese, the prediabetic curve that is seen in many obese persons, and the clinical observation that patients suffering from prolonged cachexia gain weight more rapidly when insulin is given. He suggests that the development of obesity follows a vicious circle, somewhat like this:



Spence (104) observed that in old age, there is a diminished glucose tolerance curve. He felt that this indicated that the carbohydrate storage became impaired

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as age advanced. Ogilvie (86) consequently rearranged his calculations on the basis of age and the duration of the obesity. He found that in cases of obesity under eleven years duration, there was a normal glucose tolerance; after eleven years duration there was a high percentage of decreased glucose tolerance curves. During the first five years of the obesity, one-third of the cases showed an increased tolerance. Ogilvie (86) demonstrated on autopsy material that in the pancreas of the obese and non obese subjects, there was, in the obese subjects, a definite increase in the size but a decrease in the number of the Isles of Langerhaus. From this work, Ogilvie concluded that in obesity there was a definite hypertrophy of the Isles of Langerhaus because of the stimulation of increased carbohydrate ingestion. The extra insulin thus secreted caused an increased appetite with the development of obesity. After a prolonged period of hypertrophy, there came a time when the islet tissue decompensated. At this time, diabetes is likely to develop. This concept explains the close relationship of obesity and diabetes.

However, there are several objections to this rather ingenious theory of obesity. Silver and Bauer (103) and Gardiner-Hill (40) both point out that the symptoms

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of hyperinsulinism are a tendency to fits, low blood sugar, with immediate relief by taking food. Obesity is uncommon in subjects in whom adenoma of the pancreas is present. The recently devised insulin shock therapy used for schizophrenia has not produced obesity in these patients, who are given massive doses of insulin six days a week for many months. However, Poulton (92) says that the objection that hyperinsulinism in the obese should also cause insulin shock is answered by the fact that fat persons are in reality hyperthyroids. Insulin shock is much harder to produce in the hyperthyroid. In experimental animals, insulin shock may be more readily induced following a thyroidectomy.

Wilder, Smith, and Sandiford (125) maintain that the observation that insulin is a good fattening agent is incorrect. They believe that the fattening action comes from the increased appetite due to hypoglycemia. They report that in three cases of endogenous obesity losing weight on a reduction diet, the use of 60 units of insulin per day for the period of one month was not effective in preventing the weight loss due to the reduction diet.

Rony and Levy (98) feel that the inconsistency of the results on blood sugar determinations was too great

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to postulate any insulin theory of obesity. Later, Rony and Cheng (97) determined the level of blood fat preceding and after a fat meal and found an alimentary rise. Then they injected insulin and found that in a starving dog, there was no effect on the blood fat level, but after the meal, the insulin prevented the normal alimentary rise. However, they found that the same effect could be accomplished by the administration of intravenous glucose. The administration of epinephrine, which is supposed to antagonize insulin, together with insulin showed the same effect as the insulin alone. From this they concluded that the prevention of alimentary lipemia by insulin must rest in the tissue cells themselves because adrenalin did not check the action of the insulin. They believed that an increased glycogen formation caused an increased deposit of fat in the tissues. Insulin causes increased glycogen formation in the liver. Intravenous glucose has the same effect on glycogen formation because it stimulates the liver by the rise in blood sugar concentration.

Rony (96) also tried to demonstrate the relationship of obesity to diabetes, but in following the glucose tolerance curves of twenty patients with obesity for periods ranging from one to nine years, he found that

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none of these cases developed diabetes. Repeated glucose tolerance tests showed no change over their original tests. At least six of these patients did not restrict their diet in any way. Rony questions strongly the relationship of diabetes and obesity as pointed out by Joslin and others.

Nervous Origin of Obesity

There is a very old idea and one discarded for a long time by clinician and laboratory worker alike that there is a fat center in the brain that has to do with the regulation of body weight, much as there are centers in the brain for the control of temperature, vomiting, heart rate, etc. This idea of a central regulation of metabolism again seems to be evolving in the literature. This theory postulates that damage to this center causes a change in metabolism and allows the development of obesity.

P.E. Smith (106) showed that damaging the hypothalamus in the region of the tuber cinereum, without extirpation of the pituitary gland, resulted in a tremendous development of obesity in rats. For example, in the case of two rats, one of which was operated on soon after birth, at the end of two months, the non operated rat weighed 299 grams, while the operated rat weighed 340 grams.

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In the obese rat there was also extensive atrophy of the sex glands. Smith also demonstrated that the removal of the pituitary gland did not result in obesity so long as there was no damage to the hypothalamus. Camus, Gournay, and LeGrand (18) say that the nucleus damaged in the production of obesity is the paraventricular nucleus. This is one of the four masses of cells in the tuber cinereum. Camus and Roussy (19) state that obesity never results from a lesion confined to the pituitary, but is always due to a lesion in the tuber cinereum.

Cushing (25), on the other hand, believes that the pituitary gland is most important in the development of obesity. He says that the confusion of symptoms is because endocrine obesity is almost always a pluriglandular disease. The pathology starts in one gland, and the effect of its altered secretion is to throw the whole endocrine balance over so that bizarre effects not fitting into the symptom complex for any one endocrine gland are often seen.

Carlson (20) also believes that pituitary obesity should be called cerebral obesity, because it is due to some lesion in the hypothalamus, not to underfunction of the pituitary gland. Foster and Benninghoven (37) repeated Smith's experiments and were also able to pro-

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duce artificial obesity in rats.

Bernhardt (11) believed that there was a weight regulating center in the hypothalamus in back of the tuber cinereum which formed a physiological unit with the pituitary gland. He says, "Many lesions and changes in the different organs are apt to bring out a tendency for gaining weight, but weight will change only if the central regulation fails." Bernhardt points as evidence to the fact that obesity sometimes follows encephalitis, and that only about 50% of the cases of bilateral removal of the ovaries in young women resulted in the development of obesity.

Mazier and Goldstein (78) hold that Fröhlich's syndrome is due to a concomitant involvement of the pituitary gland and the tuber cinereum. They use as evidence the fact that adiposogenitalis dystrophica occurs most frequently in suprasellar tumors which press on the hypothalamus. They also point out that in Simmond's disease where the function of the pituitary gland is in part destroyed by organic lesion, no obesity develops. Rather, the picture is one of acute emaciation, cachexia, and death.

Brain and Strauss (75) say that adiposogenital dystrophy may be encountered accompanying either a chromo-

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phobe adenoma of the pituitary or suprapituitary tumor. They say that either of these tumors results in an internal hydrocephalus, with the floor of the third ventricle becoming distended and pressing downward on the sella turcica and the metabolic centers of the hypothalamus. They say that it is hard to tell whether the pressure is active on the hypothalamus or the pituitary or both.

Adiposis Dolorosa (Dercum's Disease)

This syndrome is placed under the obesities of nervous origin because the chief symptom other than the obesity is pain. Its classification, and even its status as a clinical entity, are much debated.

Dercum (28) first described this condition in 1892. In describing his fourth case (autopsy) in 1902, he says, "The patient is a single white male, age 39. He is a man much below normal stature, his height being only four feet, ten inches. He presents a striking appearance because of numerous accumulations of fatty tissue over the entire trunk. The abdomen is so pendulous that the genitals are concealed as though by an apron. Huge folds of the fat also hang from the sides of the trunk. The deposits of fat in the arms are not as great as the deposits in the trunk. This is also true of the deposits

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of fat in the thighs and legs. Everywhere these masses of fat are exquisitely painful to pressure. The pain is most pronounced over the left side of the trunk and left shoulder. The skin is dry." Dercum believed that his disease was due to atrophy of the thyroid gland. This case however also showed marked enlargement of the pituitary, while the three previous cases had shown only the thyroid pathology. All cases showed an interstitial neuritis in the fat tissue.

Maddox (72) describes the clinical syndrome of this disease, as follows:

1. Occurs at or near the menopause
2. Fat distribution--two types
 - a. Localized painful fatty tumors, occurring mostly on the trunk and limbs
 - b. Generalized type with pendulous apron hanging from abdomen and thighs.
3. Pain--varying from occasional tenderness to constant agony.
4. Hemorrhages, ecchymosis, absence or profusion of sweating--sympathetic nervous system.
5. Mental features--asthenia, depression, melancholia instability, epilepsy, mental confusion, and true dementia.
6. Definite family history.

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The theories as to the etiology of this disease are numerous. According to Maddox (72), they are:

1. The lesion is a subacute focal inflammation in the fat with peripheral neuritis secondary to infection elsewhere. A complex network of nerve fibers can be demonstrated around the fat cells.

2. The disease may be a derangement of the diencephalic centers controlling fat metabolism. There is also a derangement of the suprarenal gland to account for the asthenia, and some pathology in the thalamus to account for the pain.

3. The disease may be a thyroid or pituitary dysphagia of unknown nature.

Wilson (127) states that this disease is not a clinical entity. It is a lipomatosis or simple obesity associated with a neurosis or neurasthenia. He reviews the literature finding 16 cases reported with autopsy. Two of these cases showed no change in the ductless glands, eight showed pituitary changes, twelve showed an abnormal thyroid, nine showed sex gland involvement, and three showed suprarenal involvement. Cushing (25) believes that this condition is a menopausal disorder.

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Because it is a human characteristic to blame the furnace instead of the stoker, and because of the oft repeated observation that in spite of the fact that we all overeat, but only a small percentage of us become obese, a great many investigators have turned their attention to the operation of the furnace, i.e. the study of the metabolism. The great bulk of this work has been to determine what differences, if any, can be demonstrated between the metabolism of the obese and the normal group. Some determinations of the metabolism in the underweight must also be included because, as seems logical, obesity and thinness represent but two extremes of the same problem.

This question has already been discussed briefly under the section on the exogenous nature of obesity under etiology. In this section, the same problems will be presented in greater detail, giving the experimental proof for the various theories. This section will include a discussion of the basal metabolic rate and possible modifications of it, the specific dynamic action of the food, the respiratory quotient, water and salt metabolism, and the much debated question of luxury consumption.

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Basal Metabolic Rate

Because of the popular belief among both the laity and physicians that obese people are frequently "small eaters," but have some mystic power of handling food more economically than the normal persons, a good many investigators have studied the problem of the basal metabolic rate in the obese in the hope to demonstrate that the combustion process was lower in them, and that they therefore developed excess weight on the normal caloric intake.

The early work in this field is not very reliable because of inadequate methods of comparing stout persons with normal controls. DuBois (31) says that in determining whether the heat production of a stout individual is above or below normal, there is obviously an error if the total oxygen consumption is compared with that of smaller men, because a large proportion of the tissue cells of the fat individual are nothing but inert fat which probably has little or no active metabolism. The error is only a little less marked if kilograms of body weight are used. The surface area seems to give the best method of comparison.

Up to 1915, German investigators did practically all the work on obesity, and they used Meeh's formula.

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Meeh's (82) formula is as follows:

$$\text{Wt. in Kg.}^{2/3} \times 12.312 = \text{sq. decimeters of body surface.}$$

DuBois (31) points out that Meeh's formula is unsatisfactory for comparison of normal and obese persons because it neglects the factor of height. It is obvious that a thin man, 6 ft, 2 in. tall, weighing 165 pounds, would have a much larger surface area and a greater metabolism than a stout man of the same weight, who is only 5 ft. tall. The same criticism applies to all formulae based on weight alone.

DuBois and DuBois (32) in 1915 devised the linear formula for determining surface area, thus:

$$\text{Surface Area} = W^{0.425} \times H^{0.725} \times 71.84$$

Where

W--wt. in kg.

H--ht. in cm.

They showed that this formula checked within 1.7% in normal persons, and in one obese woman checked to a plus 2%. They also devised a height-weight chart, that also checked to about 2%, slightly less accurate than the formula.

With DuBois's more reliable linear formula at hand, many investigators attempted further studies on the basal

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metabolic rate in the obese. In 1902, Max Rubner (100) had already compared the metabolism of a boy who was obese with that of his brother, who was a year older, but thin. They were the children of parents of small means and would not naturally be overfed. Each boy was given a maintenance diet (one which balanced his metabolism without adding to or subtracting from his body weight.) The general results of this oft quoted experiment are given below:

	Fat Boy	Thin Boy
Age	10	11
Wt in Kilograms	41	26
Total Calories of Metabolism	1 786.1	1352.1
Calories / Kilo	43.6	52
Calories / Sq. Meter.	1321	1290

These tables show that the fat boy actually had a higher metabolic rate per square meter than did his thinner brother.

Means (81) using DuBois's formula compared the basal metabolism of each subject with an appropriate standard for his age and sex, and noted the percentage variation from the standard. The first group contains subjects less than 60% overweight, and the other over 60% overweight. In the former group the actual metabolism is only 0.3% below the average. In the group, more than 60% obese, the basal metabolic rate is 2.3% below stand-

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ard average.

Group	No. Subjects	Normal Cal./Sq.Mt./Hr.	Obese Cal./Sq.Mt./Hr.	% Deviation From Standard
Under 60% ^{Over-} _{Weight}	5	34.9	34.8	-0.3%
Over 60% ^{Over-} _{Weight}	7	39.3	38.4	-2.3%

Boothby and Sandiford (13), in their remarkable summary of the basal metabolic data on 8,614 cases, showed that in 94 cases of obesity, 80% of the females and 83% of the males fell within the normal range (between plus and minus 10%.) They compared these results with 102 cases of normal individuals in good health and found that 95% of the females and 90% of the males to be within the same normal range. Only two of the obese cases were below minus 20%, and three cases were between minus 16% and minus 20%.

Strouse, Wang, and Dye (112) have compared the basal metabolism of normal men and women with a large number of underweight and grossly overweight persons. They found practically no difference in the calories per square meter of surface, and came to the conclusion that neither excessive underweight nor excessive overweight is associated with constant change in basal metabolism.

Strang and Evans (108) believe that a minus basal metabolic rate never occurs in obesity, because basal metabolic rate calculations should be made on the ideal

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surface area (as if the patient were of normal size and shape according to age, sex, and height) instead of the actual observed surface area. Like DuBois, these authors believe that fat is inert tissue and not active in metabolism. Their results calculated on this basis show that an obese subject, 83% overweight with a 29% increased surface area, used 73 calories per hour or a 26% excess over the amount calculated on observed surface area. They studied seven other subjects with similar results. When these patients were put on a reduction diet, they showed a drop in B.M.R. in most cases. Normal persons, out on the same reduction diet, showed a much greater drop in B.M.R. These authors concluded that the drop in basal rate in the obese was much less than in the normal because it represents only a drop to the normal level of these patients before they became obese.

Rony (95), in studying fifty cases of obesity, also calculated their basal metabolic rates according to ideal surface area, and, of course, found that it was always elevated. He suggested that these determinations should be called the basal metabolic ratio. He pointed out that lean persons always have a negative ratio, while obese persons always have a positive ratio. Rony, however, claimed that fat was an active tissue with active

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metabolism, and also believed that the increased work of the heart and respiratory muscles was important in this increased rate.

Wohl and Ettelson (129) found in the study of the metabolic rate in 52 cases of obesity, that the distribution in the various percentages was so irregular as to be of no use in determining the etiology of the condition.

The theory that the basal metabolic rate is lowered in obesity has been definitely disproven since the establishment of reliable standards in 1915. Regarding the idea that the B.M.R. is always elevated when calculated on the ideal surface area, this writer feels that the supporters of this idea must first prove the inertness of fat tissue in metabolism.

Modifications of the Basal Metabolism

The mere determination of the basal metabolism of subjects who are already obese is in many cases purely static in its nature and gives us only the end results of an obese condition already established. Determinations of the B.M.R. are made fourteen hours after the last food was taken presumably at a time when there is little active deposit of fat. As was shown above there is no constant change in the metabolic rate in

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the obese. The question then arises that granting the obese person has no abnormality in his metabolic rate, does he derive more energy from an identical amount of foodstuff than the non obese, or does he possess the ability to handle his food stuff more economically in its combustion in muscular exercise?

In regard to the second of these questions, Gesler (42) found that obese persons have a greater mechanical efficiency in performing a piece of mechanical work. He determined the metabolic rate (by the oxygen consumption method) on thirteen normal and eight obese patients before and after the performance of a piece of mechanical work on a special kind of hand apparatus. His results showed that the obese group (which ranged in age from 16 to 44 years) had an 18.2% to 28.1% mechanical efficiency, while the normal group (age 17 to 44 years) had a mechanical efficiency of only 15.2% to 23.5%.

However, because of the common observation that fat people "have to be good natured because they can't run and they can't fight," Wang, Strouse and Morton (120) also compared the muscular efficiency of the obese and normal individuals. In a series of careful studies on twenty-seven obese women, nine normal women, and

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seven thin women, they determined the metabolic rate in the post-absorptive condition, and during and after exercise on a bicycle ergometer. Their results showed that the obese group had a lesser mechanical efficiency than the normal and thin groups, and also that there was a decrease in mechanical efficiency as the percentage of obesity increased. Their results were as follows:

Group	% Weight Variation	% Mechanical Efficiency
Obese	94.3 - 110.1% Overweight	17.7%
Obese	30.0 - 77.2% "	22.1%
Obese	12.2 - 30.0% "	24.5%
Normal	- 10% - + 10%	24.4%
Thin	- 10% - - 23.4%	29.6%

Continuing their studies, Wang, Strouse and Smith (121) investigated the effect of fatigue on muscular efficiency in the thin, normal, and obese groups. They allowed their subjects to run the bicycle ergometer until they felt tired. Then their metabolic rate was determined and the length of time on the ergometer noted. They found that the mechanical efficiency in the obese group dropped to 19.1%, in the normal group to 21.3% and in the thin group to 23.1%. However the normal group showed a greater degree of endurance than the thin and obese groups; the endurance in the normal group being 22.3 minutes, in the thin group 15.4 minutes and in the obese group 7.1 minutes.

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From these two papers, Wang and Strouse concluded that Gessler's theory of economy of energy by the obese during work could not be supported. They suggested that Gessler's results might be due to the fact that his subjects were thoroughly trained before the experiment.

Another interesting theory of the effect of muscular work on the metabolic rate of overweight persons was postulated by Bernhardt (11). In measuring the basal metabolic rate at short intervals throughout the day he found that there were periods when it was markedly less than in the morning (the usual time for basal metabolic determinations.) He called these periods "negative phases." Pickworth (90) also noticed these periods in studying the basal rate on normal subjects during sleep, reading, partial attention to surroundings, normal diet, while sitting in an easy chair with voluntary relaxation, and during periods of irritation.

Bernhardt studied in particular the effect of exercise on the metabolic rate, and constructed a chart from his results. (See Fig. 1.) Bernhardt states that these negative phases occur most noticeably in the time following light muscular effort and after certain foods. Heavy labor shows no such results. These negative phases all last longer than one or two hours, and so may be

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very important in the energy intake and energy outgo balance of the obese individual. Normal and thin persons also show these negative periods, but not so frequently nor so markedly as the obese patient does.

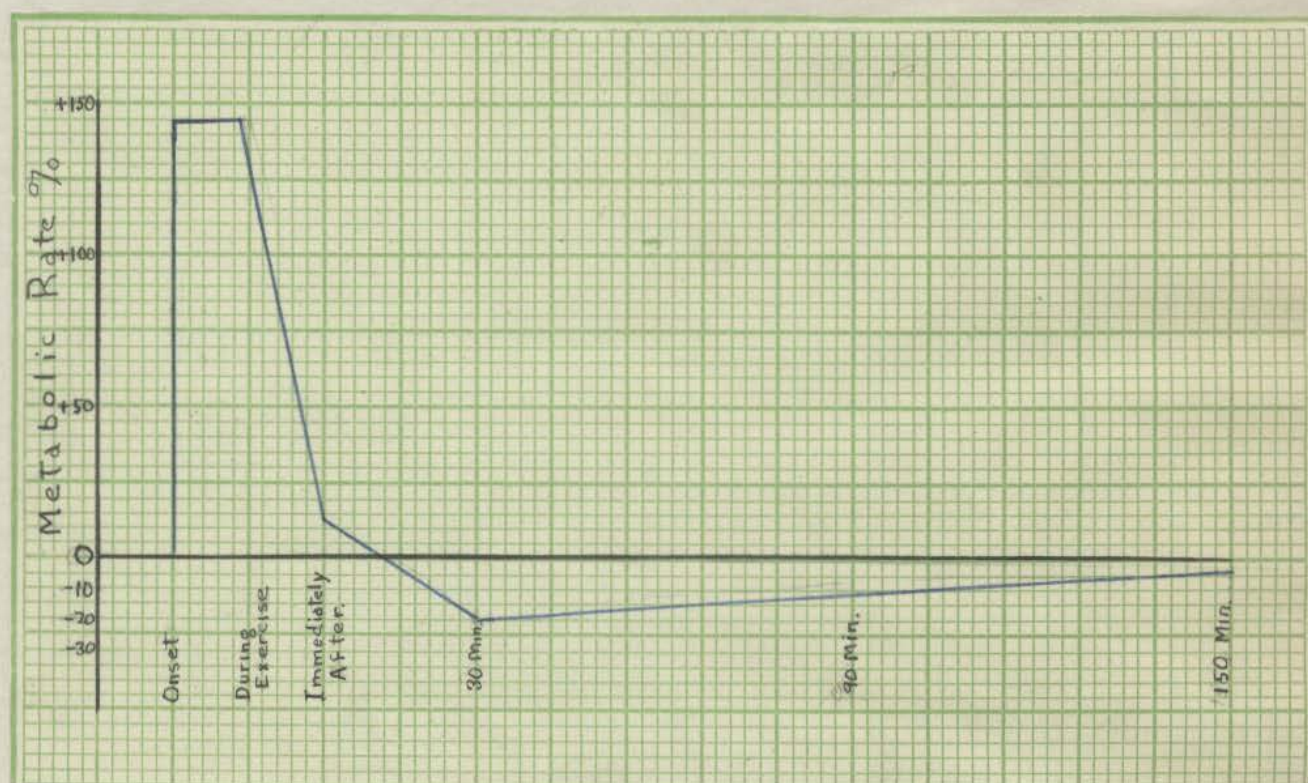


Figure 1. Negative Phases in Metabolism
(after Bernhardt (11))

Bernhardt explained his theory on the following observations. On two occasions when the routine morning basal 1. The clinical observation that many obese patients fail to lose weight on diets insufficient to maintain even their basal metabolism. He quotes a case of obesity that failed to lose weight on a 1500 calorie diet with

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fluids restricted to 800 cc and salt limited to 7-8 grams. Frequent basal metabolic determinations on this individual showed many shallow but prolonged negative phases. This subject also attempted to aid in his reduction regime by walking several miles to and from work each day, the very kind of light muscular effort which is prone to cause these negative phases.

2. The clinical observation that many persons lose weight better on a low calorie diet and rest instead of a low calorie diet and light exercise.

3. The clinical observations that convalescents from disease in which there has been a marked wasting process show a rapid gain in weight. Bernhardt says that this last group show even more profound periods of negative phase than the obese group.

Wilder, Smith, and Sandiford (125) attempted to duplicate Bernhardt's experiments. In a careful study of six obese cases, they found negative phases in one instance where the tightness of the mask was questionable, and on two occasions when the routine morning basal metabolism had been higher than the average for these two subjects. They compared both light muscular effort (flexing each leg twenty times on the abdomen) and heavy muscular effort (peddling a bicycle ergometer

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for twenty minutes.) Neither experiment showed any evidence of negative phase except the three questionable instances mentioned above.

Wang, Strouse, and Smith (122) prolonged their metabolic determinations after exercise for thirty minutes and found that in all three groups (obese, normal, and thin) the average heat production was within 1% of the normal after that time. Their results were as follows:

Group	Onset, after 30 min. Rest	During Exercise	15 min. after Exercise	30 min. after Exercise
Obese	- 4.8 %	+ 392.0 %	+ 6.5 %	+ 0.9 %
Normal	- 5.9 %	+ 404.7 %	+ 3.1 %	+ 0.8 %
Thin	- 1.2 %	+ 392.7 %	+ 6.8 %	+ 0.1 %

Benedict and Carpenter (8) in their original and early work on basal metabolic determinations, pointed out the difficulty of the determining the true base line in basal metabolism studies. Benedict says, "As our own unfortunate experiences only too frequently show, it is imperative that trained subjects be used, that there is an absolute absence of external muscular activity, that the subject be awake, that the measurement of the basal metabolism and the metabolism after ingestion of food occur on the same day, and that there is a careful check on the inaccuracies of the apparatus, including spirometer, valves, face mask, etc."

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Examination of Benedict's tables show no evidence of negative phases after meals consisting of beef tea, carbohydrate, or fat.

Strang, and McClugage (109) report a negative phase in two of their normal and three of their obese cases. However this depression did not occur in any case until five to seven hours after the ingestion of food. Also the maximum drop was only 1.7 calories or about 3% in the B.M.R. These authors conclude that there is no evidence of negative phases in the obese subjects, and the apparent depressions found by Bernhardt and by themselves were due to abnormal elevation of the base line. Benedict has already been quoted regarding the difficulty in determining this base line.

This writer is inclined to agree with later authors than Bernhardt's idea is unsound, and due to an elevation of the base line. Regarding an increased muscular efficiency, one has only to watch a fat women struggling up some stairs or a fat man running for a street car to disprove this theory.

Specific Dynamic Action

In the previous section, the question was raised regarding the ability of the obese to use their food stuff more efficiently than the normal, and it was

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concluded that they possessed no such special ability. This section will consider the other possibility, i.e. does the obese person possess the ability to derive more calories from the food stuff during its ingestion and deposition in the tissues? The most common method of answering this question is a comparison of the specific dynamic effect of various foodstuffs in the obese and normal subject.

Rubner (100) first showed that extra heat was produced during the digestion and oxidation of protein, glucose and fat. He showed that this heat was waste heat and could not be utilized by the organism for the production of muscular work; in other words the amount of energy that was necessary to perform the work of ingestion and metabolism of the food. Mason (75) gives the following values as the normal specific dynamic effect for the various foodstuffs:

Protein = 20.46% of the calories ingested in the first four hours after the protein meal.

Carbohydrate = 4.9% of calories ingested in the first four hours after a carbohydrate meal.

Fat = 5.2% of calories ingested in first four hours after a fat meal.

Jaquet and Svenson (54) in 1900 first observed a

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diminished specific dynamic action in obesity. In three cases of obesity a mixed meal, they showed that the rise in heat production was less and of shorter duration than in their normal controls. of fat, 200 grams of bread and 500 Rolly (94) was fortunate enough to make a double test on the same individual. He determined the extra heat production following a test meal of 1000 grams of raw meat and the yolk of one egg both before and after obesity developed. The basal metabolic rate was unchanged in the two tests. However, the specific dynamic effect was much decreased after the individual had become fat. (See Fig. 2.)

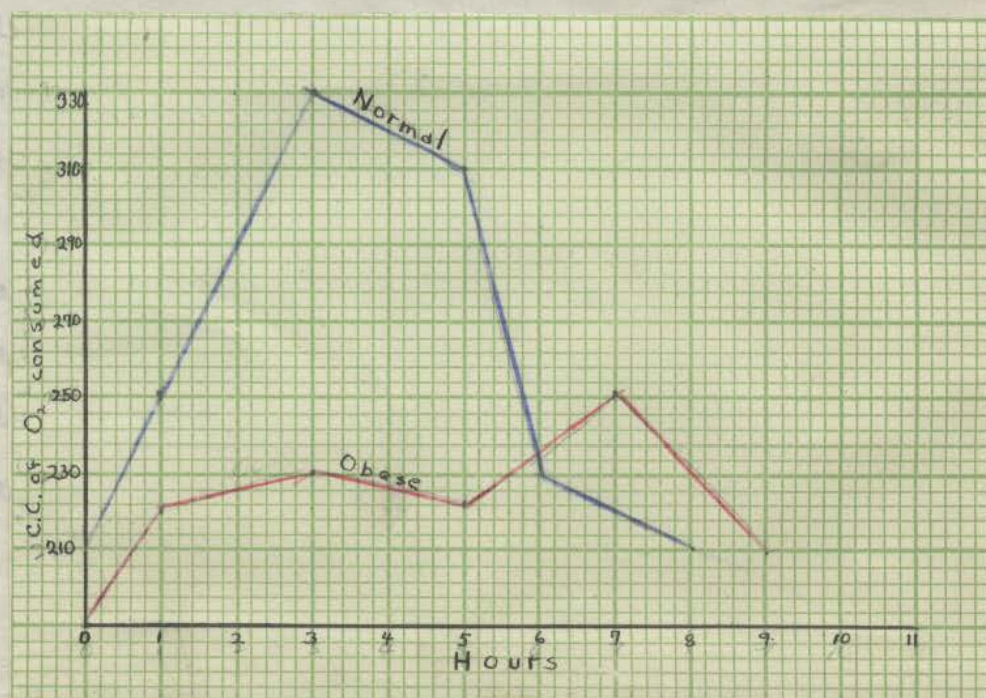


Figure 2. Specific Dynamic Effect before and after Obesity developed.
(After Rolly (94))

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A diminished specific dynamic action was also noted by Plaut (91). He studied twelve cases of constitutional obesity, giving them a mixed meal containing 200 grams of minced beef, 50 grams of fat, 200 grams of bread and 500 cc of coffee. In eleven of these cases, he found a decreased heat production as compared with the control group.

This subject has been studied in some detail by Wang, Strouse and Saunders (118). They found that in the obese subject the greatest depression of the curve of extra heat production following pure meals occurred after the administration of protein. They found relatively slight changes between the thin, normal and obese groups after carbohydrate and fat meals. They studied twelve cases of obesity, five undernourished cases, and five normal cases. Metabolic determinations were made with a Tissot apparatus at two hour intervals for eight hours following protein, carbohydrate, and fat meals. A basal determination was made in the morning before the meals. The composition of the meals were thus:

I Protein Meal--32-66 grams of minced meat

II Carbohydrate Meal--100 grams of sucrose in 50 cc
Lemonade

III Fat Meal--20% cream and butter on 50 grams toast

(See the results of these experiments, Fig. 3.)

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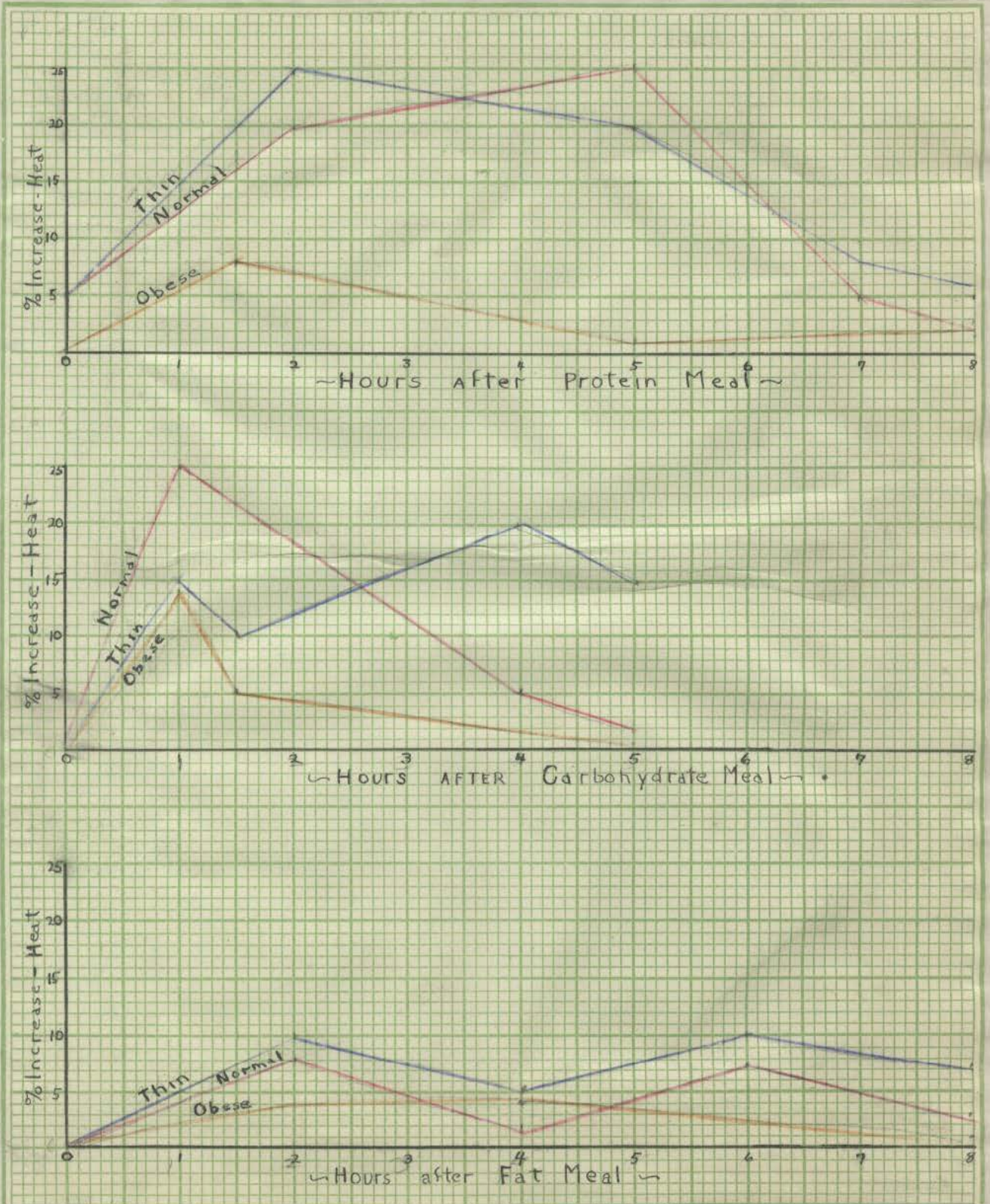


Figure 3. Specific Dynamic Effect after Pure Meals
(After Wang, Strouse, and Saunders
(118))

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Concerning this specific dynamic effect of protein in the obese, these authors say, "After ingestion of protein, obese people have a tendency to derive their energy from carbohydrate, where thin and normal people use less carbohydrate, than they do in the resting condition. Calories derived from fat in the obese tend to decrease after the meal, but show little change in the thin or normal groups. These two latter groups, however, show a decided rise in calories derived from protein after the meal. The protein consumption is little affected in the obese. This confirms our previous finding that there is very little specific dynamic action of protein in obese people."

Mason (74) also reports a diminished specific dynamic effect after a protein meal. Nine normal cases showed an average specific dynamic effect of 20.8%, while ten cases of simple obesity showed an average of 8.96%. None of these ten cases was over 15%. One case included in the obese group was a man of normal weight who had reduced two years previously. His increased heat production amounted to 6.1%, showing that this type of reaction tends to persist even after return to normal weight. Mason also found that in five cases of obesity with clinical evidence of hypopituitarism,

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the average specific dynamic effect was only 6.1%, thus indicating that this effect occurs also in the so called endogenous group.

Mason (75) also studied the specific dynamic effect in six children suffering from malnutrition. He found that the specific dynamic effect for protein varied from 16 to 30%, for fat from 25.4 to 47.6%, and for carbohydrate from 8 to 50.2%. All of these figures show an increased action of heat production in undernutrition. Re-checks after they had regained normal weight showed normal values.

Bernhardt (11) also found a marked decrease in the specific dynamic action of food in obesity, but he found that sometime there was a normal value, especially in those cases that offered symptoms of the hypofunction of the gonads. Bernhardt feels that his results were not consistent enough to account for obesity on this basis alone.

On the other hand, many careful workers have failed to obtain evidence of any real change. As Strang and McClugage (109) have pointed out, on an average caloric intake of 2500 calories per day, the specific dynamic effect amounts to about 6% or 150 calories. This excess amount of calories is not sufficient to account

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for the development of obesity in ten or fifteen years. To explain obesity on the basis of a diminished specific dynamic effect would require a drop at or near zero per cent. If such a drop were present, it would be easily demonstrable.

DuBois, Spencer, McClellan, and Falk (33) found that the average heat production after the ingestion of a protein meal amounted to 17% on the average for three normal men, and 13% on the average for four obese men. However, it was observed that the curve of heat production was more uniform in the normal than in the obese group. In the obese cases, the heat production often surpassed the normal cases after the fourth hour. DuBois, et al. concluded that while the obese man responds to protein more irregularly than the normal man, his extra heat output is not significantly different from the normal.

Strang and McClugage (109) concluded that the development of the various nutritional states is not the result of variations in the quantities of extra heat produced by the food in these individuals. They studied five normal cases, five thin cases, and eight obese. They gave a mixed meal, consisting of Protein 40 gm, Carbohydrate, 52 gm. and Fat 25 gm. They followed the

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the heat production for ten hours and found an average increase of 15% for the thin subjects, 11% for the normal, and 8% for the obese. More important, however, they felt was their observation that the peak of the specific dynamic action seemed to appear within the first hour in the thin and normal group and not till the second hour in the obese group. The effect of this on the appetite has been already discussed in the section on Etiology. (See Fig. 4.)

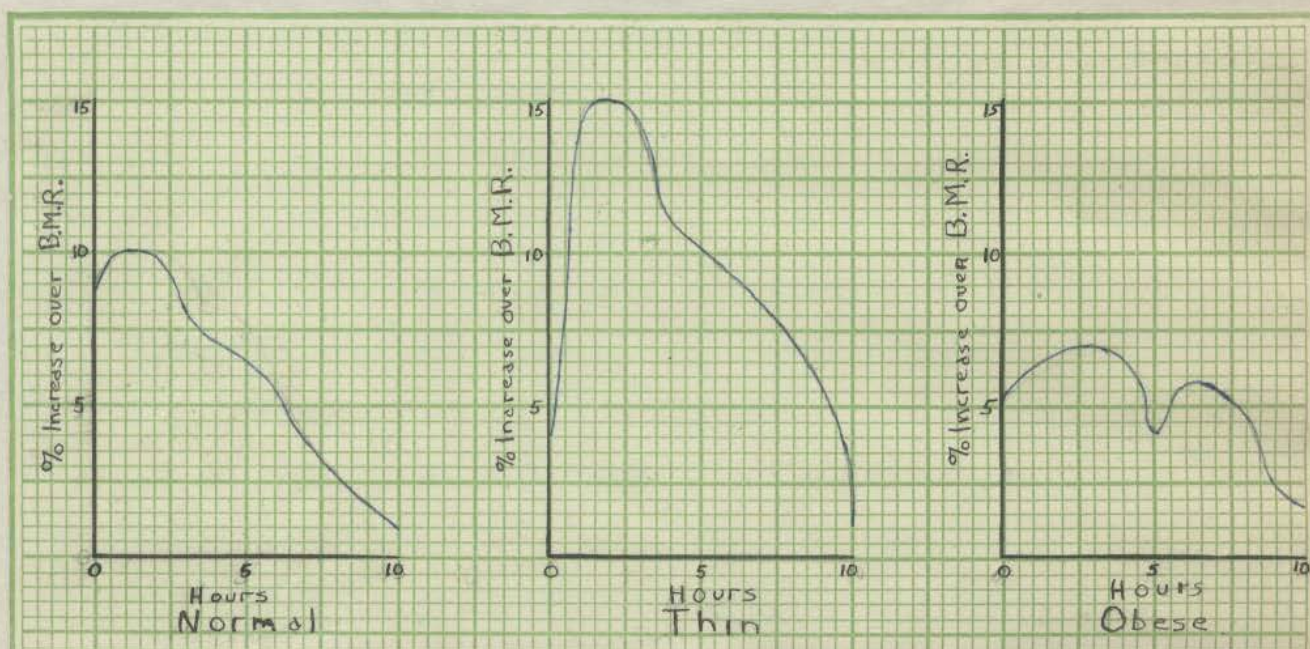


Figure 4. The Rate of Specific Dynamic Action
in the Normal, Thin, Obese.
 (From Strang and McCloghage (109))

Grzeffe (45) says, "It is an error to say that as Bernhardt (11) also noted that the specific dynamic effect is concerned, only a few cases effect occurred later in the obese group. Strang and later cases of obesity can be explained in this way."

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McClugage believed that the specific dynamic effect should be calculated on a basis of ideal surface area instead of observed surface, in which case the thin would have a decreased, and the obese would have an increased heat production.

Bowen, Griffith, and Sly (14) studied the effect of a fat meal (P 2.7, F 128, C trace) on twelve normal cases, twenty cases of obesity without diabetes, and eleven cases of obesity with diabetes over a five hour period. Their results were as follows:

12 normal cases -- 26.15 cal. S.D.A.

20 obese cases -- 25.25 cal. S.D.A.

11 obese cases -- 33.60 cal. S.D.A.
with diabetes

When they recalculated their figures on the basis of surface area per hour instead of actual heat rise, the normal cases showed a 30% rise in heat production. They concluded, however, that a fat meal had no remarkable difference in effect in either the obese nor normal group except in those cases of obesity with diabetes. They made no attempt to explain the difference in the cases with diabetes.

Graefe (45) says, "It is apparent that as far as specific dynamic effect is concerned, only a few isolated cases of obesity can be explained in this way.

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If we assume that the dynamic effect in an individual who continues to take the same diet falls from 20 to 10% and assume a period of ten hour when this is effective, the difference would be insufficient in itself to permit a gain of seven to eight kilograms of weight in a year. Both of these values are within normal limits."

It is difficult to evaluate the specific dynamic effect in relationship to the development of obesity.

Too many authors have found it to be depressed to say that it is not affected. However, because this depression is usually never more than five or six percentage, this writer is inclined to agree with Graefe that the degree of lowering is insufficient to account for any marked increase in weight.

Respiratory Quotient

Some authors have postulated the idea that depression of the specific dynamic action of food as a possible explanation of the development of obesity is of little significance because it represents only the effect of an abnormal kind of diet, (High fat, High protein, etc.). They suggest rather that the development of obesity is more due to an increased tendency of the obese person to transform all varieties of foodstuff, especially carbohydrate, into fat. Their studies have been more con-

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cerned with the distribution of energy production after food, and these investigations were carried out by observations on the respiratory quotient in both obese and normal groups.

Lyon, Dunlop, and Stewart (71) determined the respiratory quotient in many normal and obese cases on a mixed diet. They determined that the average normal R. Q. was 0.795. DuBois (31) gives 0.830. In a series of thirty-four obese cases on a maintenance diet of 2500 calories, these authors found an average respiratory quotient of 0.775. When these obese cases were put on a reduction diet of 1000 to 1200 calories, they found an average respiratory quotient of 0.721. They drew the conclusion that this low respiratory quotient in obesity could mean only one thing, incomplete oxidation. The only factors that could account for a low R. Q. is a transformation of the protein and carbohydrate to fat before it was metabolized by the body, i.e., incomplete oxidation of carbohydrate and protein. They continued **their** calculations to show that, when the protein fraction of the respiratory quotient was ruled out by determining urinary nitrogen and the non-protein respiratory quotient, according to the tables of Lusk, the average respiratory quotient was found to be 0.707. Thus the

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chief factor in the low R.Q. in obesity was due to increased transformation of carbohydrate into fat.

Bernhardt (11) noted that the respiratory quotient was diminished in his obese subjects, but also found that in some cases that it was normal or elevated. He suggested that in those cases of obesity with a high R.Q. there was a marked tendency to save fat tissue and to synthesize carbohydrate to form fat, and hence a bad prognosis as to the result of reduction diet. He observed that patients suffering from the pituitary and cerebral types of obesity had a marked tendency to have a low respiratory quotient.

Hagedorn, Holten, and Johansen (49) also postulated the theory that in the obese there was a higher rate of transformation of carbohydrate into fat. They observed that when obese persons were given a high carbohydrate diet there was a high R.Q. immediately after the carbohydrate meal and lower than normal respiratory quotient the following morning in the post absorptive condition. In twenty normal cases, they found an average post absorptive respiratory quotient of 0.864, and in thirty-three obese cases, an average R.Q. of 0.816.

Wang, Strouse, and Saunders (119) also studied the distribution of energy production after food. They de-

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terminated the respiratory quotient under basal conditions, then fed protein, fat, and carbohydrate test meals, and determined the R.Q. every two hours for eight hours. From these values they determined the non protein respiratory quotients in an effort to determine whether more fat or carbohydrate were being burned. Their results were recorded as percentage calories of protein, carbohydrate, and fat used, as follows:

Group	Protein Meal		Carbohydrate Meal		Fat Meal	
	Basal	After Meal	Basal	After Meal	Basal	After Meal
Obese (9)	25 %	28 %	16 %	46 %	60 %	46 %
Thin (8)	20 %	35 %	27 %	29 %	50 %	51 %
Normal (5)	20 %	35 %	27 %	29 %	50 %	51 %

These figures correspond to Hagedorn's et al. results showing that the respiratory quotient rises in the obese very markedly after a carbohydrate test meal. The fat test meal shows a decided drop in the percentage of fat used. These two factors, according to these authors, indicates the tendency of fat people to store carbohydrate and fat, and their tendency to be economical in the metabolism of that fat once formed.

Bowen, Griffity, and Sly (14) determined their average respiratory quotients in the normal and obese groups; finding the average normal value to be 0.825, and the average obese value to be 0.767. They fed a high fat

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meal (F 128, P 217, C trace) to six thin, six normal, and thirty-one obese individuals, with the following results:

Group	Fasting	After Fat Meal.		
		1 Hr.	2 Hr.	3 Hr.
Thin	0.815	0.824	0.800	0.810
Normal	0.825	0.824	0.800	0.810
Obese	0.765	0.762	0.805	0.790

From these figures, Bowen et al. concluded that because both groups tended to approach an R. Q. value of 0.800 both derived their extra energy for the specific dynamic action from the combustion of similar mixtures of carbohydrate and fat. This conclusion is opposed to the theory of Strouse et al. (112), who believe that the obese person tends to burn carbohydrate and spare his fat tissues. Bowen admits that his results are difficult of interpretation, but feels that the fat meal requires a certain amount of carbohydrate to be liberated from its store house.

Regarding the effect of exercise on the respiratory quotient in the obese, Wilder, Smith, and Sandiford (125) found, as might be expected, that the respiratory quotients were elevated during or immediately after exercise but were lower than normal while resting or while on reduction diets. They explained this on the basis of

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a quickened ventilation and consequent removal of carbon dioxide from the blood. The return of the respiratory quotient was usually complete within thirty minutes after exercise. Wang, Strouse, and Smith (122) also report a lower value for the R.Q. during rest and consequent elevation after exercise, as follows:

Group	Onset	During Exercise	15 min. after Exercise	30 min. after Exercise
Obese	0.759	0.889	0.822	0.749
Normal	0.755	0.921	0.775	0.728
Thin	0.767	0.971	0.837	0.749

Stewart, Gaddie, and Dunlop (107) showed that the respiratory quotient rose from the normal value to about unity for amounts of work up to 5000 kilogram meters, and thereafter fell steadily with increasing amounts of work. Further analysis, eliminating the protein R.Q., showed that the protein was not used, and that carbohydrate was used at the onset of exercise and fat at the end of exercise.

Krantz and Means (63) attempted to accentuate the difference in the basal metabolic rate between the normal and obese individual by the use of epinephrine. On the basis of the observation that thin people are nervous and emotional, and fat ones seldom so, they believed that psychic stimuli should cause a much more marked elevation of the metabolic rate in the thin person than in

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the obese. They used injections of adrenalin as a "controlled" psychic stimuli. 0.6 mgm. of epinephrine were injected and the B.M.R., respiratory rate, R.Q. pulse rate, pulse pressure were taken at 10, 20, 30, 60, 90, 120, and 150 minutes after the injection. Although there was no significant difference in the basal metabolic rate as the result of this experiment, there was a marked difference in the percentage elevation of the respiratory quotient. In the obese group the elevation was only 11.2% and in the normal group, 19.6%. These authors believe that this indicated that the increase in metabolism in the obese is met by a relatively greater oxidation of fat and less of carbohydrate than in normal people.

Stimulated by these experiments, Krantz and Means (63) studied the effect of epinephrin on the partition of food stuffs in the obese and normal. Their results were as follows:

1. Protein--no effect except with massive dose
2. Fat and Carbohydrate

- a. Pre-injection period

1. Obese--fat metabolized more than carb.
2. Normal- " " equal to "

- b. 10 min. after injection

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1. Obese--fat metabolized equal to carb.

2. Normal- " " less than "

c. 60 min. after injection

1. Obese--same as preinjection period

2. Normal- " " " "

Krantz and Means explained these results in this way, "The epinephrin stimulates the liver to give up its glycogen. The obese have a diminished glycogen reserve so cannot respond as well as normal persons do. Therefore, their respiratory quotient remains lower. Just what causes a decrease in the glycogen storage in the liver of the obese and a corresponding increase in fat deposition in the liver is not clear."

The depression of the respiratory quotient seems well established by all of these authors, but their interpretation of it seems to differ greatly. It seems to this writer that the respiratory quotient is lower in the obese persons because he has a greater proportion of fat to live on than the normal person.

Luxus Consumption

The discussion of the effect of the ingestion of food in the obese person cannot be completed without some consideration of the interesting theory of Graefe's which he chose to call luxus consumption. Excess nutrition

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is the most common occurrence in our modern civilization. It can be truthfully asserted that most people eat much more than they require. Many authors have therefore raised the question, "Why, then, is obesity not much more common?"

One of the most astonishing facts in the realm of nutrition is the ability of the healthy individual to keep his weight at a constant normal level not varying so much as a pound for ten or twenty years, in spite of wide fluctuations in caloric intake from day to day. The organism must possess some defense mechanism which prevents great accumulation fat. Obesity must be due to the break down of this mechanism.

There are two common explanations regarding this mechanism. Most authors believe that this fine adjustment of energy intake and outgo depends on the appetite and the feeling of satiety. They say that exogenous obesity may be due to faulty habits of appetite, and that endogenous obesity may be due to the inhibitory effect of certain endocrine secretions on the action of the appetite and the feeling of satiety. However, many more authors have attempted to explain this phenomenon of gain in weight on a decreased ability of the food to stimulate metabolism and consequently leave

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more calories to be deposited as fat, or a peculiar muscular economy in obese persons which enables them to burn calories more completely thus deriving more energy from them with a consequent excess of calories. All of these factors have been discussed above.

Graefe and Graham (46) in 1911 postulated a new theory which they called "luxus consumption." Benedict (8) in a very detailed study of the effect of prolonged fasting, showed that there was a striking tendency for the basal metabolic rate to decrease as the fast progressed. In a careful study on a human subject who fasted for thirty-one days without taking any food at all except a minimum amount of water, Benedict showed that his basal metabolic rate, calculated both by the direct and by the indirect method fell steadily until the twentieth day of the fast. From that time on until the end of his fast, the basal rate was maintained at this new low level. This decrease in the basal metabolism is another of the highly specialized protective mechanisms of the body. Because there is an insufficient energy intake, the body metabolism adapts itself to this new condition by lowering the rate at which food is metabolized. As the nutrition is improved, the metabolic rate rises to its original "normal" level.

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Graefe (46), therefore, postulated the idea that, if the body is able to adapt itself to continued under-nutrition by a fall in B.M.R., then the body must also be able to adapt itself to continued overnutrition by an elevation in the metabolic rate. He called this rise in metabolism, luxury consumption or in German "luxus konsumption." In normal individuals, luxury consumption is one of the normal physiological body processes. But in the obese person there is a diminished or even totally absent luxury consumption. Thinness may also be explained as an overactivity of luxury consumption.

Graefe (45) in his text book describes the work of some of the early authors in the field of metabolism, indicating that they also had found evidence of luxury consumption. Frerichs and Lehmann (38) in 1846 said that any protein over and above the amount required by the muscles was superfluous and that it had to be burned immediately. They even called this phenomenon "luxury consumption." Bischoff and Voit (10) in 1860 in their work on nitrogen balance disproved this idea that all the protein ingested had to be burned immediately.

They showed that part of the excess protein at least was stored in the body as fat. Rubner (100) in 1902, who first described the specific dynamic action of protein,

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showed that continued surplus ingestion of protein continued from day to day increased its oxidation in the body tremendously so that there was very little gain in weight. In other words, Rubner showed that if a certain excess amount of protein was given on one day, there was an elevation of the total metabolism, i.e. specific dynamic effect. If, on the second day, the same excess amount of protein was given as on the first day, there was a greater rise in total heat production. He called this the secondary specific dynamic effect. Graefe says that this in reality is luxury consumption.

Graefe and Graham (46) offered the following experiment as proof of their theory. After a preliminary starvation period of 14 days, they fed a group of dogs a mixed diet and demonstrated a terrific increase in the metabolic rate. His results are quoted below:

Days on Diet	Wt. in Kg.	Calories of Heat/24 Hrs.	B. M. R.
Beginning	20.15	1056	54 %
14 Days - Starvation	15.00	672	0 %
7 " - 2243 Cal.	18.50	816	19 %
29 " - 2580 "	20.25	1047	53 %
17 " - 1659 "	20.17	1112	62 %
19 " - 1120 "	20.00	1061	55 %
10 " - 882 "	18.50	837	22 %
7 " - Starvation	17.50	856	25 %
2 " - Unrestricted	21.00	1005	48 %

Graefe believed that this luxury consumption depended

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on the proper level of function of the thyroid gland. Luxus consumption does not continue to operate in dogs after thyroidectomy. Graefe felt that this relationship of the thyroid gland and luxus consumption might serve as a bridge between simple and endocrine obesity.

Helmreich and Wagner (52) studied the basal metabolism of normal children first on a maintenance diet and later on an overnutrition diet (with an excess of 1200 to 1900 calories.) They found that during the period of overnutrition, the basal metabolism was appreciably elevated, as follows:

After excess fat-----6-18%

After excess sugar-----6-18%

After excess protein--14-25%

These values in children certainly look like luxus consumption. Helmreich believes that there is no absolute level of basal metabolism, but that the metabolism is a function of the condition of nourishment. He believes that the cells establish their expenditures according to their stored reserves.

Graefe's theory of luxus consumption did not prove to be a very popular one. The consensus of opinion, according to DuBois (31), is that, while this theory sounds very logical on paper, one experiment on dogs

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is not significant, and that the burden of further proof must rest on the proponents of this theory.

Lusk (69) concluded that the heat loss attributed to luxus consumption is essentially the additional specific dynamic action of this extra foodstuff. He called this "delayed specific dynamic effect." Krauss and Kuppers (64) concluded that chronic undernutrition could depress the basal metabolism as much as 25% below the normal standard, and that it takes fourteen days of excessive feeding to cause this depression to disappear. They felt that Graefe's rise in metabolic rate was in reality a return to normal because he took as his normal rate, the B.M.R. as determined after the dogs had been starved for fourteen days. Graefe (45) in his textbook says of Krauss and Kuppers that they consider as pathological only such values as deviate from the normal by a plus or minus 25%. They do not report on the specific dynamic action of their diets, and consequently their work cannot be considered as significant. It seems to this writer that Krauss and Kuppers have hit on the weak spot in Graefe's experiments, and he doesn't know how to answer them. Graefe says of Rubner that he can call luxus consumption "delayed primary specific dynamic effect" or any other term that he may choose.

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Wiley and Newburgh (126) investigated the subject of luxus consumption rather carefully. They also pointed out that Graefe's experiments were done on starved dogs, and that he took as his base line, the metabolic rate as it had already been lowered to compensate for undernutrition. They said that what Graefe called luxus consumption was in reality only a return of the metabolic rate to normal. Newburgh studied a pathologically thin subject (height 6', 2" -- weight 124#.) This subject on a maintenance diet had a basal metabolic rate of -11.5% to -8.0% . When he was put on a super maintenance diet for sixteen days, he gained 8.9 pounds and his basal metabolic rate rose to -6.9% to -4.1% . On a maintenance diet again, his weight returned to 124 pounds and his basal metabolic rate to -10% . Newburgh feels that the slight increase in metabolic rate can be attributed to the increase in surface area, plus the extra specific dynamic effect of the greater diet. Graefe (45) says of this work that Newburgh failed to measure the specific dynamic effect of his diet at all and so cannot attribute his rise to it. Also, Graefe states he never claimed that luxus consumption could explain all cases of obesity nor that it occurred in all people. Newburgh's case constituted the exception that

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proved the rule. Graefe also justifies his own figures on the starving dogs by saying that the high figures of 48 to 62% after overnutrition are about 50% above the normal metabolic rate in dogs of like age and size.

Keeton and Bone (58) studied nine obese patients on a reduction diet, checking their basal metabolic rates weekly. They found that all cases stayed within plus or minus 10% of the normal figures. Strang, McClugage, and Brownlee (110) studied the problem from the other side, determining the effect of forced feeding on the basal metabolic rate in nineteen cases of severe malnutrition. They found that on the average, the metabolic rate of the group was plus 5% before the period of forced feeding and plus 3% after this period. This certainly does not look like luxury consumption. However in six of their patients, in which the gain in weight was in excess of five kilograms, there was a distinct tendency for the metabolism to rise (from 57.1 cal/hr initial to 61.1 cal/hr. final.) These authors calculated that this increase of four calories per hour corresponded to an increase in the B.M.R. of 7%, and that the surface area of these patients increased 8%. The weight increase, however, was 22%. Therefore Strang et al. feel that these figures indicate that the increase in basal meta-

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bolic rate parallels the surface area and not the increase in body weight, and that the increase in metabolism was no more than could be accounted for by the surface area. Hence the principle of luxury consumption does not appear applicable to the basal metabolism. The only extra heat influence which was attributed to the excess food intake was the additional specific dynamic action of the excess food. In other words, these authors agree with Lusk.

Observations on Water Metabolism

There is another factor which plays an important part in obesity. The surplus weight cannot be put down to fat without further investigation. Water makes up a large part of the weight, and in every case, its presence hampers up in estimating the actual fat tissue in the obese person. Water retention is a most hampering problem in reduction cures on submaintenance diets.

Pubner (101) noted that in tissues only a portion of the total water as determined by drying to constant weight, was converted into ice when the tissues were cooled to -20° C. He contented that the water which did not freeze was "bound" in the tissues. The balance of water was called "free" water. When it was observed that it was impossible to predict the rate of loss of

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weight in an obese person on a quantitative subcalorie diet, many observers indicated that this uneven weight loss was due to water retention in the fat tissue. Newburgh and Johnston (85) showed that in a normal individual on a submaintenance diet of 1078 calories, with a predicted weight loss of 95 grams a day, he actually gained 115 grams in the first five days of the diet. As the low calorie diet was continued, this subject lost weight more rapidly than the predicted weight after the first five days so that at the end of seventeen days, he had lost as much weight as predicted. Further calculations on this patient's day to day record showed that each day's weight gain or loss could be accounted for by the predicted weight loss plus (or minus) the weight of the urine, stool, carbon dioxide output and oxygen intake, and the insensible perspiration, i.e. the water and carbon dioxide lost from the skin and the lungs. Benedict and Root (9) also point out the significance of this insensible perspiration. They define it as the gaseous emanations from the body which do not appear in the form of sensible moisture or sweat, i.e. gases from the lungs, and moisture and carbon dioxide from the skin. In the normal person, Benedict and Root give the following composition to this insensible per-

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spiration.

- a. 15% of all CO₂ lost from the body
- b. 85% of all water lost from the body.

The normal rate of insensible perspiration is 25-400 grams per hour.

Rowntree and Brunsting (99) report two cases of obesity in young women who failed to lose weight on reduction regimens, but who lost weight rapidly on a reduction diet plus dehydration therapy (with ammonium chloride, mersalyl, and restricted fluid intake.)

Wohl and Ettelson (129) studied this question of water retention in obesity, and decided that in a large percentage of obese cases, there was a definite tendency to store water. These authors ran a Volhard dilution test (1500 cc of water on an empty stomach and the urine collected at hourly intervals for four hours) on thirty-six patients all of whom were at least 10% overweight. They found that 19% of these cases had a total output at the end of the four hours that was greater than 1500 cc, 28% had an output at or about 1500 cc, but 53% had an output that was smaller than 1500 cc. The average output of this last group was only 515 cc. These authors also recommended the use of the McClure and Aldrich test for the detection of obese patients with

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a tendency to store water. This test consists of the injection of 0.2 cc of normal saline intradermally on the flexor surfaces of the arms, inner surfaces of the thighs, gluteal region and on the abdomen. If the wheal persists for 60 minutes or longer, the patients were considered to have a normal rate of water absorption. Applying this method to fifteen cases of obesity, they found that:

40% showed a rapid absorption with a decreased excretion according to the Volhard Method.

40% showed a rapid absorption with a normal excretion according to the Volhard Method.

20% showed a normal absorption rate with normal excretion according to the Volhard Method.

Malamund (73) reports on fourteen cases of obesity, 82% of whom showed evidence of water retention after a Volhard dilution test. Brown and Kieth (16) report that the blood and plasma volumes when compared to the body weight are smaller in the obese than in the normal person. They compared three cases of obesity with an average for normal cases.

	Blood Plasma	Blood Volume
Normal Cases	42-54 cc	77-94 cc
Obese Case #1	36 cc	35 cc
Obese " #2	39 cc	38 cc
Obese " #3	47 cc	36 cc

These authors suggest that smaller volumes might be due to water retention in the tissues of the obese.

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Bartels and Blum (4), on the other hand, were unable to duplicate Wohl's results. They ran a similar Volhard dilution test (1500 cc of water with a dry breakfast, and collected the urine for four hours.) They compared normal, overweight, and underweight groups, with the following results:

Group	1 Hr.	2 Hr.	3 Hr.	4 Hr.	Total 4 Hr. Output
Normal -10% - +10%	389 cc	545 cc	311 cc	88 cc	1,343 cc
Obese - +10%	359 cc	490 cc	296 cc	119 cc	1,269 cc
Thin -10%	338 cc	498 cc	272 cc	57 cc	1,179 cc

Bartels and Blum concluded that the obese subject showed not a water retention, but a tendency to have a sustained output, i.e. the fourth hour output is greater in the obese group. However, the obese subject on a reduction diet showed an even more irregular water output, due to upset water metabolism.

Bernhardt (11) concluded that there was no retention of water in obesity because the specific gravity of fat people is lower than that of normal persons, e.g. the ease with which fat people float in the swimming pool. Graefe (45) says that analysis of the fluid content of fat runs all the way from 5% to 71%. The more pronounced the obesity, the lower the percentage of water. Foster and Benninghoven (37) found that the water content

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of the carcasses of rats, in which they had produced obesity experimentally by puncture of the hypothalamus, averaged between 29 and 44%, while in the normal control animals, the average water content was 62 to 65%.

It is the opinion of the writer that as yet the evidence concerning water retention in obesity seems to indicate that it is more important from a therapeutic standpoint than an etiological one. No evidence of its role in etiology has been accumulated except the observation that in an individual who has recently become obese, there is a higher percentage of water than in the individual who has been obese for a long time.

CLASSIFICATION

The classification of obesity is the most difficult part of the subject. As in the study of any disease process, the classification is useful only as it helps us to make a diagnosis of the variety of the disease process with which we are dealing. Only in this way can the treatment be applied in a scientific and logical manner. As a general rule, the most desirable type of classification is based on the etiology. However, in any disease in which the etiology is only partially understood, such a classification is of little value. Then we must fall back on clinical classifications, etc. to tide us over until the etiology is better understood.

So it is in obesity, in which, in spite of a great deal of investigation, no clear idea of the etiology is yet known. Whether or not, obesity represents a disease process in itself or is only a symptom of underlying disease processes is not known. While most of the modern workers agree that obesity represents a disease of metabolism, most of their voluminous investigation on metabolism has demonstrated only that certain factors of metabolism such as the basal metabolic rate are not the cause of obesity. No one has yet been able to demonstrate successfully any metabolic factor which is the cause of

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obesity. However this may be so only because our methods and techniques of studying metabolism are limited. The chief method of studying metabolism today is by the heat output of the body determined by the respiratory gas exchange. As yet no good laboratory procedures for the study of enzyme action, the metabolism of various tissue cells such as muscle, connective tissue, etc. have been established. Why could not a faulty action of tissue enzymes be postulated as a cause of obesity just as well as a faulty rate of heat production? As yet we know nothing of the kinds of tissue enzymes and their normal actions, let alone any idea of possible pathological action. Therefore until some constant metabolic or endocrine disturbance can be demonstrated to be associated with obesity, we can set up no good classification of obesity. However, we must work with the material at hand, and attempt to set up some temporary classification until such time as a permanent classification can be established.

Von Noorden (116) was the first to separate obese patients into two groups on an etiological basis. He said that individuals became obese either because they ate too much and exercised too little, or because they had some alteration of metabolism which slowed up the

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rate of their metabolic processes, and allowed obesity to develop. He called the first group exogenous obesity, and the second group endogenous obesity. Now this was a very useful classification and has become the classical type. Some of the many authors who have followed this classification are quoted below.

Gauss (41) furnishes a typical example of this type.

- I Exogenous--due to too much food or too little exercise.
- II Endogenous--associated with various endocrine disturbances.
 - a. Hypothyroid
 - b. Hypopituitary--Fröhlich's syndrome.
 - c. Hypogonadism
 - d. Pluriglandular
 - e. Cerebral
 - 1. Dercum's disease
 - 2. Lipomatosis

Coombs (24) lists the same classification of obesity but separates the lipomatosis into a separate group.

- I Alimentary (exogenous)
- II Endocrine (endogenous)
- III Lipomatosis (localized accumulation)

Neither of these two classifications are of much value to the clinician because they do not offer any good method for determining to which class a particular patient belongs. Hunter (53) says that obesity should be divided into two classes; one in which no organic lesion can be demonstrated, and the other in which or-

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ganic pathology can be found:

- I No organic lesion--hyperialimentation
- II Organic Lesion--demonstrated by certain symptom complexes.
 - a. Hypothalamic--history of encephalitis, hypersomnolence, lethargy, genital atrophy
 - b. Fröhlich type--hypopituitary state occurring in adolescents, characterized by obesity and genital atrophy
 - c. Suprasellar cysts--headache, blindness, xray of sella turcica
 - d. Suprarenal--virilism, hirsutism, muscular development
 - e. Dercum's type--painful areas of fat, progressive weakness and psychosis
 - f. Cushing's type--pluriglandular--florrid face, purple striae and typical distribution of fat over the anterior portion of the body.
 - g. Myxedema--middle aged women, slow mentality, wooden expression of the face, dry hair, scaling skin, slow pulse, low temperature.

Weber (123) gives much the same type of classification but differentiates his types according to characteristic fat distribution.

- I Exogenous obesity--excessive intake of food.
 - a. Plethoric form--generalized distribution of fat, healthy appearance, hemo. % = 120%
 - b. Anemic form--generalized distribution of fat, which is edematous in appearance, low hemo. % = 30%
- II Endogenous obesity--glandular disturbance plus a large appetite.
 - a. Hypothyroid--generalized distribution of fat, with a peculiar type of subdermal infiltration with fat pads at ankles, neck, wrists, and nuchal areas
 - b. Abnormal pituitary--fat distribution is limited to the middle portion of the body (breasts, abdomen, buttocks, thighs, and spindle fingers.)

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- c. Hypogonadism--trochanteric distribution of fat.
- d. Adiposis dolorosa--more or less localized accumulations of fat with painful areas in this fat.
- e. Suprarenalism--fat is distributed over abdomen, chest, face, associated with hirsutism, and masculizing syndrome.
- f. Pluriglandular--fat distribution is atypical, but tends to follow the fat distribution that is typical of the endocrine gland that is most altered.

Bernhardt (11) believes this is a good method of differentiating the types obesity. He points out that the different endocrine glands do not influence the subcutaneous tissues of the whole body in the same degree. The thyroid is more active in the upper parts of the body, the gonads are more active in the hips, girdle and lower extremity. This phenomenon is a remnant of the original metameric structure of the body. Barr (3), on the other hand, points out that this system falls down because the so called "girdle" type of obesity is found in either pituitary or hypothalamic lesions. This particular objection may be answered on the basis that the so called "pituitary" obesity may be due to pressure on the hypothalamus, as pointed out by Mazier and Goldstein (78). Graefe (45) too says that fat distribution is useful in only about 20% of the cases in which the obesity is typical and sharply defined.

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Many other authors have modified von Noorden's original classification somewhat. They believe that obesity should be divided into three great classes, instead of two. Typical of this group is McLester (79).

- I Alimentary obesity
 - a. Hereditary tendency
 - b. Failure of the body mechanism which prevents obesity in the normal person
- II Constitutional type--altered metabolism
 - a. Respiratory quotient indicates that obese person burns fats less readily than normal
 - b. Decreased specific dynamic effect of protein.
- III Endocrine obesity
 - a. Dercum's disease--pituitary-thyroid disease
 - b. Dystrophica adiposa genitalis--Fröhlich's Syndrome
 - c. Hypothyroid condition
 - d. Hypogonadism
 - e. Pineal and suprarenal glands
 - f. Lipomatosis

Lambie (65) gives the same classification with a little different wording.

- I Developmental--hereditary obesity
- II Nutritional--wholly acquired
- III Metabolic--constitutional (Both hereditary and acquired.)
 - a. Endocrine
 - b. Neurogenic
 - c. Neuro-endocrine

Newburgh and Johnston (85), the great exponents of the purely exogenous nature of obesity, have classified this condition according to appetite.

- I Perverted habit--persons who overeat because

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- a Neglect stimulus of feeling satiety
- b Trained to overeat by obese parents
- c Nervous, weak willed persons--like chronic alcoholics
- II Decreased activity--persons in which food habits have become set to a certain level of activity, and who continue to eat the same amount of food in spite of lowered energy requirement.
 - a Occupation requiring less energy
 - b Lowered basal metabolic rate because of hypothyroidism and other endocrine disturbances.

Rony (95) believes that all forms of obesity depend on a constitutional tendency and classifies them accordingly.

- I True obese person--one who who maintains an increased weight and continues to maintain it except for incidental loss due to disease or undue strain, and in whom the weight is restored to normal obese state when conditions are restored to normal.
 - a. Dynamic--in which there is a tendency to gain weight. This phase is most active just after reduction of weight due to a restricted diet.
 - b. Static--no tendency to gain in weight.
- II Masked Obesity--persons who maintain a normal weight by artificial means such as living on a restricted diet.
- III Pseudo Obesity--persons who are overweight temporarily due to forced overnutrition and limited exercise.

Bernhardt (11) who believes that the development of obesity depends on the failure of a fat regulatory center in the hypothalamus, offers this classification.

- I Obesity as the result of primary disturbance of the central regulation of metabolism
 - a. Pure cerebral form--encephalitis, tumor

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- b. Pure pituitary disturbances
 - c. Mixed form
- II Obesity as a result of secondary functional disturbances of the central regulation of metabolism.
 - a. Endogenous factors
 - 1. Disturbances of general behavior--hunger, thirst, activity.
 - 2. Disturbances of endocrine glands
 - (a) Single glands--thyroid, gonad, adrenal, pancreas pineal
 - (b) Pluriglandular disease.
 - 3. Disturbances of the periphery--primary lipogenic tendency of the tissues.
 - b. Exogenous factors
 - 1. Overeating
 - 2. Muscular inactivity
 - 3. Mixed forms.

Some authors have classified obesity in relationship to age of onset. Tidy (113), Engelbach (35), and Christie (23) are the chief supporters of this group. Christie's classification is as follows:

- I Infantile
 - a. Exogenous
 - b. Hypothyroid (cretinism)
- II Juvenile
 - a. 50% pituitary or thyropituitary
 - b. 50% endocrine imbalance of temporary nature.
- III Adult
 - a. 90% exogenous
 - 1. Men--after marriage, after prosperity
 - 2. Women--after growth stops, after pregnancy
 - b. 10% endogenous--hypogonadism, pluriglandular disease.

In writing this paper, this author has been struck

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with the necessity for some laboratory procedure that could be applied clinically and that would aid in the treatment of the patient, even if it did not give a clear indication as to the etiology of the obesity. John (55) had some such idea in mind when he separated obesity into exogenous, endogenous, and constitutional on the basis of the metabolic rate.

- I Exogenous obesity--normal B.M.R. with obvious hyperalimentation
- II Endogenous obesity--decreased B.M.R. This may be due to hypofunction of the thyroid, pituitary, or gonads.
- III Constitutional obesity--decreased diet causes no loss of weight, with normal B.M.R.

Kern (59) supports this type of classification. Haussleiter (51) divides endogenous obesity into three types: normal, elevated, and decreased basal metabolic rate. This classification is not sound because as Wohl and Ettelson (129) found, the distribution of the cases of obesity in the various percentages of the B.M.R. is so irregular and inconstant as to be of no use in determining the etiology of the condition. Rony (95), Strang and Evans (108) pointed out that the B.M.R. was always elevated in the obese when calculated on the basis of the active tissue, considering fat tissue to be inactive.

Bernhardt (11) in studying the respiratory quotient

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in obesity found that there were two classes.

- I Elevated R.Q.--in these patients, there was a marked tendency to spare fat tissue and so gave a bad prognosis as to the loss of weight
- II Normal or low R.Q.--good prognosis for losing weight.

This might be a useful test, but too many authors (Hagedorn, Holten and Johansen (49), Wang, Strouse, and Saunders (119), Lyon, Dunlop, and Stewart (71), and Du-Bois (31)) have shown that the average respiratory quotient was lower than normal in the obese. Only in a very small percentage of the cases was it elevated sufficiently to make this test of any significance.

Wohl (128) points out that in some cases of obesity there is a tendency to **store** water. By means of the McClure-Aldrich test, which consists of the intracutaneous injection of 0.8% sol'n of NaCl in the flexor surface of the forearm, inner surface of the thigh, gluteal region, and abdomen, and noting the rate at which the wheal tends to disappear, an indication of the tendency of any case of obesity to store water can be determined. When the wheal persists for sixty minutes, no increased tissue avidity for water exists. Wohl reports on fifteen cases in which 80% of them showed an increased rate of absorption of water. Why,

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then cannot we classify obesity thus:

- I With Water Retention
- II Without Water Retention

This is a very simple clinical test and might prove very valuable. Those patients with a tendency to store water would be treated by a reduction diet plus a restricted fluid and salt intake. Newburgh and Johnston (85) report on several cases of obesity treated in this way in which they could predict the weight loss per day. This might explain also many cases of the so called constitutional obesity who fail to lose weight on a reduction diet for a time. Newburgh believes that all constitutional cases represent only water retention.

SUMMARY

From a review of library material covering the literature of the past three decades on the subject of obesity, the following facts pertaining to the etiology, metabolism, and classification may be summarized.

1. Obesity is always the result of a positive energy balance whether this be predominantly due to exogenous or endogenous factors.
2. Exogenous and endogenous factors are so intimately related that no given case of obesity can be classified as due to one or the other.
3. Certain cases can be assumed to be predominantly exogenous, i.e. those due to overeating, lack of exercise or both.
4. Certain other cases can be assumed to be predominately endogenous, i.e. those with some evidence of obscure internal disease. This class includes hereditary, endocrinopathy, and central nervous system disturbances which factors probably control body weight by influencing the appetite, feeling of satiety, and bodily activity through some interrelated mechanism of control.
5. Studies of the metabolism indicates that as yet no consistent metabolic disturbances, as determined

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by our present methods, have been demonstrated in more or less constant association with obesity.

a. B.M.R.--the vast majority of cases of obesity fall within normal limits as far as basal metabolic rate is concerned. The disturbance of basal metabolic rate is rare and inconstant finding in obesity.

b. The obese group is less efficient as regards muscular work. No evidence can be demonstrated for the so called "muscular economy" of the obese.

c. Specific Dynamic Action--many obese persons show a slight depression in the specific dynamic effect of protein, but this is not sufficient to account for the development of obesity.

d. Respiratory Quotient--the obese person manifests a lower R.Q. than the normal. This may mean an increased tendency to store carbohydrate. More likely, it indicates only that the obese person has a greater store of fat on which to live.

e. Luxus Consumption--the theory of luxus consumption remains a theory appearing very logical on paper but unsupported by experimental evidence

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except by Graefe.

f. Water Metabolism--probably water retention in obesity is due to an altered metabolism as the result of a reduction diet. Water retention is probably not important in the development of obesity.

6. Regarding classification, the division into exogenous and endogenous is is an artificial and dogmatic one, unsuited to clinical application because the vast majority of cases fall in the middle zone being neither entirely exogenous and endogenous

7. Better than the above, is an attempt to classify obesity on a functional basis, similar to the functional classification of heart disease. This type of classification is recommended only as a temporary measure until such time as the etiology and metabolism of obesity can be better understood.

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